

Table of Contents

XI APPENDICES	1
A. Response to Public Comments	2
B. Review of Residential History and Risk Factor Informtion for Non-Hodgkin's Lymphoma and Multiple Myeloma in the Deerfield River Valley, MA	31
C. Evaluation of Female Breast Cancer Inidence in Shelburne, MA 1982-1994	37
D. Risk Factor Information for Selected Cancer Types	55

XI APPENDICES

Response to Public Comments

Listed below are comments received from the public regarding the February 1997 Health Consultation: Cancer Incidence and Down Syndrome Prevalence in the Deerfield River Valley, Massachusetts. The public comment period originally ended in March. However, in response to requests by the DRV community, the public comment period was extended to three months, ending on May 12, 1997. The following comments are related to factual errors and have been corrected in the report.

Comment # 1: "Regarding the 21E sites section, the last paragraph on page 19 should read, "...The status of three of these sites was modified to indicate that the location was not disposal sites or did not currently require further remedial response actions. The remaining seven sites..."

Comment # 2: "The last paragraph of Page 1 states that all 17 Massachusetts towns in the Deerfield River Drainage basin are located in Berkshire County, which of course they aren't...One is in Berkshire County, one is in Hampshire County, and all the rest are in Franklin County, Massachusetts."

Comment # 3: "The first paragraph of Page 2 likewise contains an unfortunate introductory misstatement of fact-as your own Figure 1A indicates, not only does Ashfield not abut the Deerfield River, but neither does either Heath or Hawley."

Comment # 4: "Table 1B, Bladder cancer SIR = 162, but the text states the SIR as 163. Table 1B also Breast cancer exp. = 66.5, but the text says 66.9."

Comment # 5: "Regarding Table 2A: There are several SIR calculations where the observed was less than 5. These should be changed to NC. Regarding the Notes sections of all the tables...rounded to the *neareast*..." is spelled incorrectly."

Comment # 6: "Page 18, Section C, Section 1, Line 7: The term "mass spectroscopy is incorrect and should be "liquid scintillation."

Comment # 7: "Page 18, Section C, Section 1, Paragraph 2: At the end of line 5, the following should added prior to the period: "...but below the regulatory limits."

Comment # 8: "Page 18, Section C, Section 2, Paragraph 2, Line 4: We suggest deleting the number "100" and merely saying approximately 350 mrems. We also wonder whether you should delete the reference to diagnostic x-rays."

Comment # 9: "Page 25, Paragraph 3: There is a major error in the reference here, since it should be 100-600 rems rather than 100-600 mrems. This is an order of magnitude of 1000 time's higher levels to produce the effect. This error is incorrectly leading to a judgment call that 100-600 mrems is "relatively large doses of radiation."

Comment # 10: "Page 32, 9th reference: Tom O'Connell's name has two "n"s and two "l"s."

Comment # 11: "On page 3, paragraph 3 line 1, I believe the sentence should read "Specifically, an SIR is the ratio of the observed number of cancer cases to the expected number of cases multiplied by 100."

The following comments address overall or general issues in the Health Consultation. Many similar comments were received by different individuals seeking clarification of a given issue or topic. Where possible, these comments were listed together and a single response has been provided.

Comment # 12: "On page 5 your report states the reporting efficiency for Down Syndrome (DS) was only 9% in Massachusetts so it is obvious that data had to be collected by other means. However, it is not clear if the data collected are comparable to California data because the reporting methods were very different. The reporting efficiency for DS cases may be significantly different in the two studies. For example, the report states that sources such as outreach programs and the Citizen's Awareness Network (CAN) 'confirmed diagnosis of DS' to you. It is not clear from the report if such diagnosis of DS is easy or reliable in all cases or if the persons making the diagnosis were trained doctors or untrained laypersons. Did physicians at the Department of Public Health reconfirm each diagnosis?"

Response: The Citizen's Awareness Network (CAN) was a significant source of information for identification of children reported with DS in the DRV area. However, cases were not confirmed by CAN. If a child reported with DS met the case definition, then parental consent was obtained to participate in the investigation and for a BEHA staff physician to review medical records for the child to confirm the diagnosis of DS. The medical records were reviewed by a MDPH physician consultant to confirm each diagnosis. The diagnoses for seven of eight children reported with DS were confirmed in this manner. The parents of the eighth child reported with DS did not respond to consent forms, but in an effort to be conservative the child was counted as a DS case, regardless.

Comment # 13: "In your letter of April 10th you state that all comments and responses will be included as an appendix to the report. We object to this approach. Since MDPH has described our relationship as a 'partnership', we believed that our comments would be reflected in the final report even if they were not mutually agreed upon."

Response: This is an MDPH report and as such it must reflect the MDPH's best technical judgment on the health outcome and environmental data evaluated. Where appropriate, changes have been made in the actual report based on public comment. We hope that CAN and other community members endorse our relationship as a partnership in that we have attempted to address all concerns and have worked with CAN to identify such concerns and data relevant to our report.

Comment # 14: "We request our hypothesis, as well as Dr. Cobb's analysis and Cindy Folkers' comments be included in the final report."

Response: The CAN hypothesis, as we understand it, is that historic releases of tritium to the Deerfield River and possibly the surrounding environment may be associated with increases in cancer and Down Syndrome (DS) in the Deerfield River Valley. This hypothesis is stated in the introduction on page one of the report.

Dr. Cobb's analysis was not cited because the conclusions are based on data that were not age-adjusted. It is critical to age-adjust incidence and mortality data in order to make valid comparisons to state and national databases.

Cindy Folkers' comments and our responses are included in the appendix of the final report.

Comment # 15: In regards to the Down Syndrome part of the study. On page 26, 1st paragraph, "the evidence of a cluster is ambiguous". The evidence is clear, only your wording and findings are ambiguous. When...I met with Dr. Larry Edmonds CDC last April, he proclaimed this finding of

3 cases of Down Syndrome within a 1/4 mile of each other and all 8 within a 3 mile area, of being a definite cluster related to an environmental pollutant."

Comment # 16: "Concerning your remarks about the geographical locations of the DS cases...These sentences obscure the fact that, out of 253 square miles covered by the 11 towns you studied, 7 of the 8 children born with DS in the 1980's were born within a three mile radius, the center of the circle being that group of houses in Buckland."

Comment # 17: "In your report you found a fourfold increase in the birth of children with DS, but you state that there was 'no apparent spatial or temporal pattern observed among these children'. I find it shocking that you could not find a spatial cluster here. The eleven towns of the study add up to 253 square miles, and the cases of DS fall within a three mile radius with 4 of the cases falling within less than 1/4 mile."

Response: MDPH will restate the wording of the conclusions to indicate the presence of a cluster of three children with DS occurring in Buckland during the 1980's. However, this will not change the primary conclusion of the report, that there was a statistically significant increase of the prevalence of children with DS in the DRV during the 1980's. It also does not affect the recommendation that if the families of children with DS, the CDC, the MDPH, and the CAN determine that follow-up investigations would lead to a better understanding of DS among these children, then the MDPH recommends that such additional investigation be conducted in cooperation with the CDC.

When we examined available information on the eight children with DS, we found that three Buckland cases occurred within a one-quarter mile area of each other, but made no comment about the proximity of all eight children to each other. Based on the mother's residence at the time of birth, as indicated on birth certificates, the eight cases occurred in an area of approximately 110 square miles.

We are unaware of the source of information that indicates that eight of the children with DS lived within a three mile radius. This may be a result of using different sources of information and a different case definition than the one used by the MDPH. For instance, community maps of children with DS might differ substantially from MDPH maps if medical abortions and stillbirths were included. Similarly, community maps may differ from MDPH maps if maternal residence at conception were used instead of maternal residence at birth.

As with cancer incidence, to determine whether elevated numbers of children with DS have occurred in the DRV, the observed number of children with DS in the DRV is compared to the number that would be expected based on the statewide experience. Because Massachusetts did not have a birth defects registry at the time this report was being prepared, data from the California birth defects registry was used as a comparison.

As discussed in the draft Health Consultation (page 4), the case definition was limited to live births to allow for a valid comparison of the prevalence of DS in the DRV to the prevalence estimates cited in the literature, reported as the number of DS cases per number of live births. In addition, the case definition did not include residence at conception because the information is not readily available and is difficult to verify.

Comment # 18: "What criteria did you use to define clusters?"

Comment # 19: "The DPH should tell us the criteria for defining "geographic proximity" or a cluster (I understand this is a difficult and sensitive determination), or refrain from concluding anything about DS cases regarding geography of occurrence."

Comment # 20: "MDPH found a fourfold increase in the birth of children with DS, however the report states that there was no 'apparent spatial or temporal pattern observed among these children'. The eleven towns add up to 253 square miles, and the cases of DS fall within a three mile radius with four of the cases falling within less than 1/4 mile. Why is this not defined as a spatial or geographical cluster? In addition, you reference a study by Rothman and Fabia, which found one case of DS for every thousand births in Franklin County from 1950-1966. Why then is this not a temporal cluster? What criteria does MDPH use to define a cluster?"

Comment # 21: "...you reference a study by Rothman and Fabia in which there was a finding of one case of DS for every thousand births right here in Franklin County during the 16 year period from 1950-1966. Even after disregarding several DS births, you acknowledge a four-fold increase in DS during the ten year time period 1980 and 1990. Common sense says that this is a temporal pattern or cluster."

Response: One common definition of a cluster by Last (3rd edition) is an "Aggregation of relatively uncommon events or diseases in space and/or time in amounts that are believed or perceived to be greater than could be expected by chance." However, epidemiology does not offer a single definition with defining parameters for cluster investigations and the MDPH did not restrict this evaluation to quantitative analysis to determine the presence of a cluster. Cluster analysis at MDPH also involves a qualitative review, which is based on experience with similar investigations over many years in Massachusetts.

MDPH will restate the wording of the conclusions to indicate the presence of a geographical cluster of three children with DS occurring in Buckland during the 1980s. However, within the time period studied, there was no clustering of cases during certain years. Therefore, evaluation of the time frame of birth for all eight children did not indicate an unusual pattern (i.e., a temporal cluster).

Because the prevalence of DS was statistically significantly elevated, the MDPH did recommend, that if the families of children with DS, the CDC, the MDPH, and the CAN determine that follow-up investigations would lead to a better understanding of DS among these children, then the MDPH recommends that such additional investigation be conducted in cooperation with the CDC. The CDC has agreed to assist with this follow-up.

Comment # 22: "These comments also apply to your recommendations on page 28, last paragraph where you state 'no unusual geographic pattern was observed among these children in relation to the environmental data'. I would rather have you state that 'a geographic clustering of the Down Syndrome cases was noted and points to the need for further studies to try to determine evidence for an environmental contaminant. These studies will be undertaken with the assistance of the US Centers of Disease Control, and other governmental agencies as deemed necessary to do adequate testing for individual factors and environmental factors.'"

Comment # 23: "Furthermore, throughout this report you state that there have been no unusual temporal and geographic patterns observed. What really bothers me about this is that based on that finding you conclude that there is no need for further environmental investigation."

Comment # 24: "If these cases are not considered spatially related, the study should clearly state just how close they would have had to have been to be considered a cluster. This finding is used as part of the reason that there is no need for an investigation of environmental factors, yet, there is no reason given to explain away the existing DS clusters."

Response: It should be clarified that the primary reason for not further investigating environmental contamination in relation to DS is that there are currently no known environmental

causes of DS. Without some knowledge of what causes DS, environmental sampling would be unfocused and difficult to interpret.

MDPH will restate the wording of the conclusions to indicate the presence of a cluster of three children with DS occurring in Buckland during the 1980s. However, this will not change the primary conclusion of the report, that there was a statistically significant increase of the prevalence of children with DS in the DRV during the 1980s.

Comment # 25: "Some sort of visual is need to show this relationship, I am certain that this can be accomplished in a manner that respects the confidentiality of the victims."

Comment # 26: "Maps of the area with the designation of cancer cases and Down syndrome cases should be provided to the Health Committee and the community. The maps could be placed in local libraries. The street names could be eliminated to protect confidentiality. If the MDPH refuses to provide us with this information, we asked that it be provided to our expert, Dr. Dick Clapp of the John Snow Institute in Boston to analyze."

Comment # 27: "We would like to see the mapping that was gathered from the Cancer Registry and plotted during the summer of 1995."

Comment # 28: "I would like the mapping information to be presented to another group of scientist who may find clusters where you see none."

Comment # 29: "In view of our questions concerning your definition of spatial clusters, we request that mapping data be provided to the Health Committee and the community. This could be easily accomplished while maintaining confidentiality by removing streets from the map. It is the Health Committee's understanding from MDPH remarks made on 2/26/97 at the public meeting that a formal request is required to gain access to this information because of MDPH protocols. We are eager to start this process and await your response."

Response: We are not able to provide such maps because the confidentiality of the cases must, by law, be protected (MGL c.111, s.111B, 105 CMR 301). Eliminating streets will not allow the address locations to remain confidential, especially in such a rural area as the DRV. Because this information is confidential, the MDPH does not have a formal request process for this data. The Massachusetts Cancer Registry does have a research protocol for organizations that wish to submit proposals to obtain confidential data for research purposes. As part of this protocol, a detailed research methodology is required and must be submitted to the Institutional Review Board for approval. The CAN may want to coordinate with John Snow Institute or other groups to discuss the feasibility of this option.

Comment # 30: "At the very least how about showing how many of the cancer cases in the 11 DRV towns occurred within the CAN boundaries versus how many in the parts of those towns not falling inside the boundaries? For those figures to be meaningful it would also be important to know the relative populations inside and outside those boundaries."

Response: In regards to the CAN boundaries, the report does state (page 15) the total number and proportion of cancer cases occurring outside of the CAN boundaries. However, meaningful population data in relation to these boundaries are not available.

Comment # 31: "Cancer is the most obvious result of an environmental problem but reproductive problems, other birth defects, learning disabilities and neurological effects were never looked at, yet they are our canaries, especially birth defects and reproductive problems."

Comment # 32: "Now that your study has revealed a very high incidence of children born with DS in the DRV, it is time to take into account the incidence of stillborn, miscarried and aborted fetuses with DS. Also of other birth defects. Please also study more generally reproductive health in the DRV as strong anecdotal evidence points to increases in sterility, miscarriages, irregular menstruation. A household survey asking a wide range of questions concerning the health of residents, including the existence of immune disorders, would be a better way to proceed than focusing only on isolated diseases. In many of the families of the children with DS at least one of the parents is suffering from serious health problems."

Comment # 33: "I think it is also important to document the incidence of major birth defects from 1982 on in our community."

Comment # 34: "Finally, other health effects, such as sterility, and birth defects other than DS, need to be evaluated in order to obtain a more accurate epidemiological picture. Low birth weight is an especially sensitive indicator of synergistic pollutant effects in humans."

Comment # 35: "Moreover the study should be expanded to encompass other birth defects in addition to the Down syndrome. There is clear anecdotal information regarding multiple birth defects, sterility, miscarriage. We again ask the MDPH to provide a letter to Dr. Grandison as promised at our meeting on 2/13 with MDPH and CDC, to help elicit support from other doctors concerning other birth defects."

Response: The MDPH agrees that it would be very helpful to track birth defects not just in the DRV, but throughout the Commonwealth in order to address questions and concerns about possible relationships between birth defects and external factors (e.g., environmental exposures). The MDPH recently initiated the Center for Birth Defects Research and Prevention with funding provided by the CDC, which will soon begin full monitoring and surveillance of the number and types of birth defects occurring in Massachusetts. Until the birth defects surveillance system is in place, however, the MDPH is not able to track more intensively in one particular area without tracking birth defects throughout the state as a whole. Comparison data are crucial in the field of epidemiology.

However, infant mortality is a universally accepted measure of the overall health status of a community and this type of data is readily available for analysis. During the 20 year period 1969 to 1989 the infant mortality rate per 1,000 live births in the DRV towns combined was 7.5, lower than the Massachusetts rate of 11.6 for the same time period. This data is presented in Appendix B, Table A-1.

Comment # 36: "I would like those involved with issuing the conclusion of this part of the study to consider using the criteria of public health significance instead of your chosen statistical significance. In our little community, which is often sparsely populated, it may not be possible to reach statistical significance, which as you state on page 3 'statistical evidence is not assessed when fewer than five cases are observed.'"

Comment # 37: "Your overall finding that there is no overall increased rate of cancer in the DRV is also puzzling. Your report acknowledges many statistically significant, near significant and higher than expected cancer rates throughout the DRV. Given our small population, and the difficulty that exists finding statistical significance in small populations, it seems that the fact that so many elevated levels of sickness were found would mean that there is indeed an increase."

Comment # 38: "In relation to breast cancer incidence in Charlemont, 8.2 cases were expected and 13 were observed. In this little community that has public health significance and should be followed up in my opinion. This increase was more from 1987-1992 as was the increase in Shelburne and warrants continued follow-up over the next 5-10 years to see if this is a trend. In

relation to Pancreatic cancer in Buckland, 2 cases were expected and 5 cases were observed. For bladder cancer in Buckland 4 cases were expected and 6 were observed. In Rowe 1 case of bladder cancer was expected and 3 were observed. In my opinion these types of cancer all need close observation over the next 10 years to see if we are just beginning to experience an increase. As I stated earlier, in our little community which is sparsely populated for the most part, these increases in cancer assume public health significance even if our numbers do not assume statistical significance."

Comment # 39: "I am writing you to urge you to further investigate the health effects of the past operation and current decommissioning of Yankee Rowe Atomic plant on the health of residents in the Deerfield River Valley (DRV)."

Response: As noted, our Health Consultation concluded that the available data do not suggest that residents of the DRV experienced excessive rates of cancer during 1982-1992. We also noted that several cancer types were elevated such as, NHL among females in Deerfield; breast cancer among Shelburne women; and multiple myeloma in the DRV overall. MDPH agrees that these findings have public health significance and thus recommended some follow-up for each of these three types of cancers. The BEHA has completed this follow-up work and the results are summarized in Appendices B and C.

Several comments mentioned other cancer types that did not reach statistical significance (e.g., Buckland would have expected four cases of bladder cancer, and six were observed). When we examine cancer incidence for any town in Massachusetts, we will frequently see situations in which the observed number of cancer cases is greater than expected. We will also frequently see situations in which the observed number of cases is less than expected. Such variation is not unusual, which is one of the reasons that statistical tests are conducted to determine whether the observed differences may be due to chance or are not likely to be due to chance. For example, our report contained many calculations of expected versus observed numbers of cancers, and for over two-thirds of these calculations, the observed number of cases was less than expected.

As correctly pointed out, for a rural area such as the DRV, for many cancer types, the number of cases is small, and the smaller the number of cases the more difficult it is to show that observed versus expected differences may be statistically significant. Nonetheless, we do not always use statistical significance as a requirement to conduct follow-up work, as is clearly demonstrated in our recommendation to conduct additional follow-up work on a non-significant elevation in multiple myeloma.

The MDPH does, however, evaluate the data in their entirety and in terms of temporal and geographic patterns. Based on our review of all the cancer types throughout the eleven towns included in the report, the MDPH believes that overall, residents in the DRV did not experience excess rates of cancer. A few cancer types warranted, in our opinion, some follow-up investigation. It is also important to note that the MCR data are updated annually and therefore increases in certain cancers can be evaluated for years following this investigation. As noted in the recommendations section in the final report, the MDPH will continue to monitor cancer incidence in the 11 DRV towns through the Massachusetts Cancer Registry.

Comment # 40: "I would also ask that you include in the report the unusual occurrence of serious illness in parents of 7 of the 8 Down Syndrome cases...It would help the individuals, who are involved, in their healing process to have their condition acknowledged in the report."

Comment # 41: "In addition, there is an important relationship between the occurrence of Downs syndrome and the additional severe medical complications that many of the families of these children are suffering. This is true for the rest of the valley as well. This phenomenon has never been investigated by the MDPH. It is a fundamental aspect of this investigation."

Response: The MDPH has offered to cooperate with the CDC to further evaluate DS in the DRV, if the families of children with DS request such follow-up. Follow-up might include evaluation of parental factors (e.g., illnesses) in addition to other factors in the children with DS. This type of detailed parental information can be evaluated as part of the follow-up investigation.

Comment # 42: "Though CAN may have failed to catch the omission of brain, prostate, colon, and rectal cancers from the list of cancers to be studied that does not mean the omission should be permanent. Given the findings of the study so far it is crucial also to study these cancers now. The United Kingdoms Atomic Energy Commission has discovered a possible link between tritium exposure and increased incidence of prostate cancer."

Comment # 43: "I think it is important to also look at colon, prostate, and brain cancer."

Comment # 44: "Given the statistical significance in cancers and Downs syndrome and the incidence of multiple myeloma, we request that MDPH analyze the statistics for brain tumors, prostate cancer, and colon/rectal cancers...Tritium, in animal research, is associated with unusual colon tumors in animals."

Response: Ten types of cancer were evaluated in this investigation. Leukemia and cancers of the lung and thyroid were selected for evaluation based on their known potential sensitivity to ionizing radiation. The remaining cancers were included in order to address current concerns raised by the CAN regarding suspected elevations in the incidence of these cancer types near the Deerfield River.

During the development of this project and in discussions between CAN and BEHA, cancers of the brain, colon, and prostate were not raised as cancers of concern by the CAN. However, we have included in this appendix the 1987-1994 MCR cancer incidence data for these cancer types in Tables A-2 through A-4. In addition, refer to Appendix F for a discussion of the known etiologies of each of these cancer types.

During the 8-year period 1987-1994, brain cancer incidence in the DRV as whole was nearly statistically significantly elevated (27 observed versus 18 expected, SIR=150, 95%CI=99-218) overall. When separated by gender, the increases were approximately equal in males and females, but were not statistically significant (males: 14 observed versus 9 expected; females: 13 observed versus 8 expected). When analyzed by town, elevations in the overall incidence could be largely attributable to an increased incidence in Ashfield and Deerfield. However, it is important to note that this incidence data was obtained from the MCR City and Town report, *Cancer Incidence in Massachusetts, 1987-1994*. This report combines two different types of cancer, brain cancer and central nervous system (CNS) cancer, into one category, brain/CNS cancer. In addition, the MCR includes reporting both benign and malignant tumors for both brain and CNS cancer. It therefore is possible that the reported increased incidence of brain cancer may be due to an overestimate of cases.

During the 8-year period 1987-1994, colon cancer incidence in the DRV as a whole occurred less than expected (84 observed versus 117 expected) overall and among females and males at the rate expected. There were no significant elevations among any of the towns when analyzed separately.

During the 8-year period 1987-1994, prostate cancer incidence in the DRV as a whole occurred at statistically significantly lower than expected rates for males (62 observed versus 83 expected; SIR=75; CI=57-96). There were no increases in any of the eleven towns.

Comment # 45: "And I would ask that Colrain be added to the 11 towns studied since we are now considering other etiologies for the possible environmental contaminants than radiation."

Colrain has been the site of some industries that were releasing toxic substances during the time period in question."

Response: The focus of the DRV Health Consultation was to answer specific questions regarding citizen reported increased cancer incidence and DS prevalence in the DRV based on concerns related to Yankee Rowe. The MDPH realizes that over time the CAN may have become aware of other environmental concerns in the DRV area. The MDPH Health Consultation was not intended to be a comprehensive review of health and the environment in the DRV, rather it was intended to evaluate concerns specific to cancer and DS in DRV towns with the primary concern being Yankee Rowe. The available data do not suggest that residents of the DRV experienced excessive rates of cancer during the period 1982-1992. Based on the findings regarding cancer and DS, the MDPH has conducted follow-up work on certain cancer types that were elevated.

The BEHA can analyze cancer incidence and the distribution of cases in the town of Colrain. However, the Colrain analysis would be independent from the DRV analysis. To perform this type of analysis a written request must be submitted to BEHA specifying the issues and cancers of concern.

Comment # 46: "I find it very odd that the DRV was found not to be an effluent pathway for the Yankee Rowe nuclear reactor."

Comment # 47: "The Committee is disturbed that after years of investigation, which included the analysis by Dr. Spengler's graduate class at Harvard School of Public Health, the MDPH states that the DRV is not the effluent pathway for the reactor (or for Deerfield Specialty located under a mile down stream from the power station). Dr. Spengler found the DRV to be the effluent pathway for the reactor over three years ago with tritium concentrations at least a 1,000 times greater within the valley than without. How could this information be excluded from your analysis?"

Response: The report does not state whether or not the DRV is considered an effluent pathway for the Yankee Rowe nuclear reactor. Furthermore, Dr. Spengler's research group did not find DRV to be the effluent pathway for the reactor, instead the group explicitly assumed that DRV was the effluent pathway in order to model the upper bound of potential human health impacts to individuals residing in the DRV.

In addition, the information that tritium levels were greater in the DRV than in unimpacted areas was included in the analysis on page 19, 1st paragraph which quotes verbatim the four conclusions of Dr. Spengler's research group.

Comment # 48: "...I wonder if you have had our (Shelburne Falls) drinking water checked."

Response: Public drinking water testing requirements and maximum contaminant levels (MCLs) are regulated by the Massachusetts Department of Environmental Protection (MDEP). The public water supply for Shelburne Falls (a.k.a. Shelburne Falls Fire District) is tested on a regular basis for bacteria, lead and copper, inorganics, nitrates, nitrites, radionuclides, secondary contaminants (recommended), synthetic organic compounds and volatile organic compounds. The latest water test results for 1996 and 1997 indicated that the public water supply for Shelburne Falls is in full compliance with all regulatory standards. Specific testing locations and results can be obtained from the MDEP (Western Region), Division of Water Supply at (413) 784-1100.

Comment # 49: "...I gather there is some controversy over the value of focusing so much on measurements of statistical significance in the area of public health and that there is an alternative concept of Public Health significance. Would you discuss this in your report?"

Response: The issue of public health significance versus statistical significance pertains to how one interprets data. We would suggest that public health significance implies a broader view of significance in that statistical significance may not be the sole criterion for further evaluation. For example, often times the consistency or plausibility of findings is also evaluated.

The DRV Health Consultation analyzes surveillance data on cancer incidence to address citizen concerns of suspected elevations. The cancer types selected for evaluation are based on the cancers of concern as specified by the citizens or because the scientific literature has suggested an environmental association with some of these cancer types may be possible. As such, the DRV report compiles information on the number of cases of disease in an area (the DRV) in comparison with the number that would be expected based on the statewide experience for that particular cancer. These data are evaluated using standard descriptive statistical tools (i.e., Standardized Incidence Ratios accompanied by 95% Confidence Intervals).

While MDPH does rely on statistical significance as a guide to further action, it is not the sole criteria, as is clearly demonstrated in our Health Consultation for the DRV where the BEHA has conducted some follow-up on a non-significant elevation in multiple myeloma. The BEHA evaluates the data in their entirety and in terms of temporal and geographic patterns. For all data, regardless of significance, MDPH evaluates factors that may influence disease occurrence such as smoking, occupation, and other information that may be available.

Based on our review of all the cancer types throughout the eleven towns included in the report, we believe that overall, residents in the DRV did not experience excess rates or unusual patterns of cancer incidence. A few cancer types warranted, in the Department's opinion, some follow-up investigation. This work has been completed and is included as Appendices B and C.

Comment # 50: "It is absurd to bring a Community Assessment Unit into Shelburne to study the incidence of breast cancer there (28 cases where 19.4 were expected) but not into Charlemont where 13 cases were observed and 8.3 expected. Charlemont and Shelburne are next door to each other. In both towns the majority of the populations live very close to the river (as opposed to, for example Conway where the population is concentrated some miles away from the river.) Please study Charlemont as well as Shelburne. Not to do so would suggest that your follow-up on these findings is a mere gesture intended to quieten local fears rather than a sincere attempt to find out what is happening."

Comment # 51: "Moreover, there are serious flaws in the analysis presented by the MDPH. While the MDPH determined that there was statistical significance in breast cancer in Shelburne and are undertaking a further study. Charlemont a few miles upstream has clear increases in breast cancer but is excluded from study because it doesn't meet the requirements for statistical significance due to small population. 13 cases of breast cancer were found while 8 were expected. This is arbitrary, capricious, and unscientific. The cases in Charlemont should be included in any investigation."

Response: The use of the Standardized Incidence Ratio and the 95% Confidence Interval are not arbitrary, but are standard statistical tools used by epidemiologists to evaluate the disease status of a population.

In addition, the current MDPH investigation did not find a statistically significant increase of breast cancer in Shelburne during 1982-1992. The MCR initially reported a significant increase in breast cancer during 1982-1990. Subsequent follow-up revealed that part of this increase was due to the miss-assignment of cases among Buckland residents to Shelburne. Although Charlemont may have had elevated rates of breast cancer, the increases in each time period were small (i.e., less than or equal to three) and did not warrant follow-up. Other towns also along the river, such as Buckland, Deerfield, Florida, Monroe, and Rowe experienced expected or lower than expected

rates of breast cancer. If studies on the environment and breast cancer, currently being conducted in other areas of Massachusetts, provide new information that may be of importance for this area, follow-up studies may be possible.

Comment # 52: "The earlier scare about the high rate of breast cancer in Shelburne -- which turned out to seem even higher than it is because residents of the town of Buckland who live in Shelburne Falls were included -- suggests you should look at the incidence of breast cancer in Shelburne Falls as an entity. Note: nowhere else in the DRV do so many people live in such close proximity to the river. Also, there might be an especially high level of exposure to contaminants such as tritium in the river if these i) evaporate from the large area of fairly still water upstream from the dam ii) are aerosolized by the large waterfalls."

Response: The MDPH did evaluate Shelburne Falls as an entity. Although SIR rates were not calculated separately for the Shelburne Falls area due to the lack of necessary population data, case specific data were evaluated for this area (i.e., data of diagnosis, stage of cancer, age at diagnosis). In addition, evaluation of the geographic distribution of cancer cases in Shelburne Falls revealed an even distribution throughout the town.

Comment # 53: "I was shocked to hear at the meeting on 2/26 that you had not reached any conclusions as to the cause of the increased incidence of cancer and Down Syndrome (DS) in the DRV. If this is indeed the case the first two sentences on page 28 seem to me to be extremely misleading. It is hardly surprising that local newspapers carried reports citing these remarks and interpreting them to mean that the DPH study had found that effluent from Yankee Rowe played no part in the increases you found here. At the public meeting you stated that it was not a part of this first study to investigate the causes of the increased incidences of cancer and DS you found and yet you felt entitled to draw conclusions about the dose of tritium received by residents and its effects."

Comment # 54: "In my opinion, given the misleading remarks in your report I have cited above, it is incumbent on you to contact local newspapers and ask them to publish an announcement to the effect that the DPH has reached no conclusions whatsoever on the possible causes of an increased cancer and Down Syndrome among residents of the DRV and that reports to the contrary resulted from inappropriate remarks made in the preliminary report."

Response: The MDPH did not state that it had reached no conclusions regarding cancer and DS. We specifically concluded that the available data do not suggest that residents of the DRV experienced excessive rates of cancer during the period 1982-1992. Regardless of the causes of DS, environmental or otherwise, the MDPH also concluded that DS was elevated and has offered to coordinate with the CDC to conduct follow-up surveys of the families of children with DS, if the families request us to do so. MDPH remains in support of these conclusions.

As is correctly pointed out, no single epidemiology study, including this one can determine cause and effect relationships. The last conclusion (pages 27-28) clearly states that "*Based on these results* it is unlikely that tritium exposures to DRV residents would result in an increase in the occurrence of cancer or Down Syndrome".

This conclusion pertains only to the available data reviewed in this report. The data reviewed include the most recent literature on the etiology of DS, the most recent literature on the health effects of exposure to low-level ionizing radiation, two health risk assessments of potential tritium exposures to DRV residents, limited residential well sampling for radionuclides, review of case medical records, geographic and temporal distribution of the children based on maternal residence at birth, and the location of 21E and TRI facilities.

The responsibility of the MDPH is to conduct investigations and provide a summary of findings in a report form. The manner in which the results and/or conclusions of the MDPH are presented or interpreted beyond that is not within our control.

Comment # 55: "In addition, we request that MDPH reference CAN's annotated bibliography on Tritium to support the carcinogenic, mutagenic, and teratogenic effects of organically bound tritium."

Response: The Health Consultation cites those documents, which were used in the preparation of the report. Several references cited in CAN's annotated bibliography are also referenced in the MDPH Health Consultation.

Comment #56: "Furthermore, you use of meteorological data is incorrect. As the health physicist for Yankee himself stated at one of the public meetings, and as most local people would have been able to tell you, wind direction may be predominantly from the north or northeast when you stand on a hill but in DRV wind mostly blows down the valley."

Comment # 57: "Fourth, the DPH report uses prevailing wind direction data from Yankee Atomic Electric Company. Since the authors did not elaborated on this data, how and where it was gathered, it is hard to assess its validity concerning the health assessment. However, I would point out that the Company did a previous (1959?) report on wind flow in the valley and discovered frequent air inversions which could act to trap airborne pollutants within the valley walls, recirculating them. I'm sure the DPH is aware of this report since they obviously had access to the MacIntosh study which uses it as a dispersion model for their risk assessment."

Response: MDPH has removed the sentences regarding the prevailing wind direction in relation to the location of the children with DS.

Comment # 58: "I also urge you to make all hydrologic, geologic, population density and other human factor information available to the public so that others might also study the data and model the fate of tritium in its HTO and OBT forms."

Response: Much of these data are already in the possession of the CAN. MDPH does not generate or collect information on hydrologic or geologic variables, but will direct all written and oral requests for publicly available data to the appropriate agencies. Also, the MDPH did not perform assessments or model the fate of tritium, but will forward any requests received to the authors of the assessments used in this report. Data from the MCR and the BEHA that would potentially identify individuals are confidential and are protected by state laws (MGL c. 111, s. 111B, 105 CMR 301).

Comment # 59: "We feel it is necessary for our scientist to review this data."

Response: Much of the data used in this report is available to the public, and, if requested, the MDPH will provide assistance in the acquisition of this data. However, MCR data regarding individual names, addresses, and diagnoses are confidential and Massachusetts's law (MGL c.111, s.111B, 105 CMR 301) prohibits disclosure. In addition, the data regarding children with DS are also confidential.

Comment # 60: "In addition, we ask that the mapping and your statistical analysis be provided to our expert, Dr. Dick Clapp of the John Snow Institute, as an independent epidemiological organization in Boston to analyze the data and confirm MDPH's lack of spatial or temporal clustering."

Response: Massachusetts state laws prevent the MDPH from disclosing this data. However, Dr. Richard Clapp may submit his own data request to the MCR if he wishes to conduct similar analysis. The MCR, which collects this data, has a protocol for organizations (or individuals) that wish to obtain this data for research purposes. As part of this protocol, a detailed research methodology is required and must be submitted to the Institutional Review Board (IRB) for approval.

Comment # 61: "Also, where is your recommendation for follow-up communication with the Deerfield River Valley Health Committee and the wider community? We who are affected by this situation need regular face to face contact with the DPH on a regular basis (perhaps every two months) in order to follow up with these recommendations. Will you recommend different contact people for families affected by DS and cancer? I think you need to write a separate recommendation to describe how communication will be achieved."

Response: Follow-up research for certain cancer types (breast, NHL, multiple myeloma) will be conducted primarily through research of existing records and databases and will not involve contact with affected individuals or their families.

The MDPH will offer to meet and discuss the results of the cancer incidence follow-up with the community upon its completion. If the families of children with DS request a follow-up study, the MDPH will co-ordinate this follow-up with the CDC and will establish contact with each family. In addition, the results of this follow-up will be shared with and presented to members of the community upon request. Furthermore, BEHA staff is always available by phone to provide updates and will return calls to residents to reduce any long-distance phone costs.

Comment # 62: "Your preliminary conclusion (page 26) is that there is no overall elevated rate of cancer. The report then acknowledges that there is statistical significance in breast cancer (nearly) and in NHL (statistically significant) and a widespread incidence multiple myeloma, but MDPH proposes to eliminate their significance by studying individual case histories instead of environmental factors since MDPH's primary conclusion is that there is no spatial or temporal clustering for anything. The DRV is a cluster in itself."

Comment # 63: "Although there is an indication that occupations were analyzed for the cases and MDPH recommends a residential and occupational history, there appears to be no investigation either into occupational history for the control group or a determination of whether individuals worked inside or outside the valley. We request that an investigation be initiated to determine occupation histories for the controls and whether the cases worked inside or outside the valley."

Comment # 64: "Your first and primary conclusion (page 26) is that there is no overall elevated rate of cancer and that there is no spatial or temporal pattern. You then acknowledge that there are some elevated rates of breast cancer and multiple myeloma, and statistical significance in NHL but you propose, as I see it, to explain them away by studying individual case histories instead of the environment since your first and primary conclusion is that there is no spatial or temporal clustering for anything."

Response: The Health Consultation was not a case-control study and therefore, there is no control group. The purpose of studying individual case histories was not to explain away cases but rather to gather additional information in order to identify factors that are known or suspected to influence disease occurrence for certain cancer types, and to determine the residential and occupational history of the individuals.

The purpose of a residential history is to determine the plausibility of an environmental exposure contributing to a person's illness. This is particularly relevant in the case of cancer because the

current state of knowledge indicates that the latency period (the period from exposure to an agent and development of disease) for most cancers take 20 to 40 years. If a resident of the DRV has been diagnosed with cancer, but has lived in the DRV for only a short period, it is less likely that an environmental exposure in the DRV played a role in the development of that cancer. Residential histories of each individual are necessary to determine if residence in a certain location for a period of time would more clearly indicate that an environmental exposure might be related to their illness.

Several cancers and diseases have been strongly associated with occupational exposures to chemicals. The purpose of an occupational history is to determine the plausibility of occupational exposures contributing to an individual's illness. One possible explanation for increases in cancer incidence in a community is if a number of individuals have occupations potentially exposing them to hazardous chemicals on a regular basis. Occupational information provided by the MCR is generally limited to the type or category of employment at the time of diagnosis and only rarely includes the address of employment which could lead to specific information on types of potential exposure. The MDPH has completed the residential and occupational histories for several cancer types. These results are presented in Appendix E.

Comment # 65: "...I think it is unacceptable to declare that there is a lung cancer case not "geographically located due to insufficient information regarding an exact residence." I'm sure there are multiple sources of that information in the town which were not tracked down, through public record avenues or otherwise—understanding that the knowledgeable source (though perhaps of a somewhat informal or personal sort) would not be hindered by the lack of street numbers in our towns at that time, and could ascertain the location or absence in our town of the person at the time in question. This, of course, is supposing that the confidentiality of the study's approach isn't so extreme that it actually hinders the study's results. To prove this assumption wrong, a comprehensive listing of the sources exhausted in these unverified cases ought to be included in the report."

Response: Please refer to the bottom of page 6 in the report. The sources used include: Massachusetts Cancer Registry database (1982-1992), the available Residents List for each town, usually located in the Town Hall or Town Library, and the Greenfield, Northampton, and North Adams area phone directories.

In addition, CAU staff spent several weeks visiting all 11 towns in order to verify address locations and to locate more densely populated areas, and characterize the distribution and types of residences on major routes.

Furthermore, confidentiality prohibits us from asking residents in the community where someone lives or may have lived. Although we were unable to map one lung cancer case, all lung cancers were included in the townwide analysis (2 cases observed versus 8.8 expected). The conclusions of the Health Consultation were not hampered by the lack of information for this address.

Comment # 66: "In soliciting input from the affected families, all agreed that a land use history, water, soil, and vegetation sampling of the cluster were an essential ingredient of any thorough analysis. Families are also interested in using the results of the environmental testing to determine the existence and levels of specific contaminants in the blood of family members since the majority of the family members are struggling with their own significant and disabling health conditions. Families remain concerned about these health problems and the very real possibility that they are suffering ongoing exposure to toxic levels of environmental contaminants. Our finding was that six families are willing to participate in the blood testing offered by the CDC in order to establish the timing for the chromosomal damage. Most of the families have agreed to the interview process although several families are concerned that the instrument is not specific to our situation. Again we urge the MDPH to commit to a multi-level family health investigation utilizing the resources of the community to directly aid you in this work."

Comment # 67: "The families with Down syndrome handed you a striking geographical cluster of birth defects for your study. We thought we were doing our civic duty and that you would be interested to investigate this. Instead you simply looked at our papers and then told us that in DPH-speak this cluster was not geographical because there was no underlying causality or hypothesis of causality. Aren't you people supposed to issue a call to action to do some detective work to look for causality, not to mention expanding the search for additional cases since our information gathering was very preliminary. No, not at all, I guess. In fact it seems that you have an opposite motivation to make it go away since you spent more time dismissing some of the cases we presented under lofty statistical scientific principles. Even with all this obfuscation on your part, the Down syndrome numbers were still high, so you included some anemic recommendations to look at family case histories instead of investigating the environment especially in the 1/4 mile area where there were four families with birth defects."

Response: Based on the data reviewed, MDPH found that there was a statistically significant increase in children with DS in the DRV during 1980-1990. From this information and consultation with Larry Edmonds, of the Centers for Disease Control (CDC), Birth Defects and Genetic Diseases Branch, Division of Birth Defects and Developmental Disabilities, it was determined that the best way to proceed was to survey the affected families. A survey of the affected families may indicate a common environmental or other factor. However, Larry Edmonds also indicated that the survey could be severely limited by recall bias, because most families will be asked to recall events that occurred more than 10 years ago. If the families of children with DS request a follow up investigation, the MDPH recommends that such additional investigation be conducted in cooperation with the CDC. The CDC has agreed to assist with this follow up.

Also, blood sampling was explored as an option to identify the type of mutation that caused the DS. The presence of a certain type of mutation lends more evidence that an environmental exposure may be related to DS in these children. However, the cause of DS remains unknown.

The primary reason for not recommending environmental investigation in relation to DS is that there are no known causes, environmental or otherwise, of DS. Without some knowledge of what causes DS (derived from large case-control studies) or additional information gained through follow-up with the affected families, environmental sampling would be unfocused and difficult to interpret.

Our investigation of cancer incidence and DS prevalence in the DRV was intended to be descriptive in nature, providing information on trends and patterns which may suggest the existence of a common etiology or may suggest an excess of well established risk factors in a certain area. It is beyond the scope of this investigation to determine if exposure to tritium, or any other factor is causally related to the development of cancer or DS.

Comment # 68: "The information on smoking is confounding and irrelevant. There is no case control. No statistics for the population at large given to provide a context for these smoking statistics. If the general population smoked as much as those with cancer then the information is irrelevant and appears to be used to undermine the data obtained. Therefore what are the statistics on smoking for the population at large."

Comment # 69: "Smoking data is meaningless unless compared with a control group."

Response: As previously stated, the Health Consultation was not a case-control study and therefore there is no control group. However, we agree that it is important to put the DRV cancer incidence smoking data in perspective. Unfortunately, estimates of smoking prevalence in the DRV are not available to compare whether smoking among individuals diagnosed with cancer in the DRV is greater or less than those not diagnosed with cancer in the DRV. However, the MDPH

is able to compare the smoking status of DRV residents diagnosed with cancer to the smoking status of individuals diagnosed with the same cancers in the state as a whole.

For comparison, the smoking status of selected cancers (e.g., lung and bronchus, bladder, kidney, and pancreas) for the Massachusetts population has been added to the report (refer to Figures 2B and 2D).

Comment # 70: "Information has been brought to our attention that the town of Whitingham, VT bordering Yankee Atomic has serious increases in cancer. We realize that MDPH will not be able to include Whitingham, VT to the study however due to its proximity to the power station and the potential for recharging and ground water contamination, the illnesses need documentation and possible referral as happened with the unusual number of cases of brain tumor in Greenfield, MA."

Response: The MDPH has contacted the Vermont Health Department and provided them with a copy of our report.

Comment # 71: "We now request a thorough investigation of hospital discharge records, blood lab files, and prenatal diagnostic records to confirm additional children with DS. This investigation should research incidence of DS in all towns included in the study. To gain a clear understanding of the time frame and whether temporal clustering exists, it is necessary to expand the years under investigation back ward to 1970 and forward to the present time. Although MDPH eliminated a number of Downs syndrome cases because they did not meet "MDPH requirements", the over all number of cases should be included in the report (11), and explanation should be provided for the removal of certain cases, and the spatial relationship acknowledged."

Response: The overall number of cases and an explanation for the removal of certain cases are included in the Health Consultation (see page 16 and Figure 3). The wording of the conclusions has been modified to reflect the spatial relationship of the children with DS whose maternal residence at birth was in Buckland. In addition, the MDPH recently established the Center for Birth Defects Research and Prevention, which will soon begin monitoring and surveillance of the number and types of birth defects occurring in Massachusetts, including the DRV area.

As explained previously, the BEHA is limited in its ability to ascertain all cases of DS from the 1970s to the present. To ascertain all the cases, it would be necessary to examine every record of a live birth in every hospital that serves all the towns in the DRV. As noted, approximately twenty hospitals serve DRV residents. BEHA staff contacted these hospitals and found that computerized records were either not available at all or only available for the most recent years. Therefore, ascertaining additional cases is not possible given the resources and readily available information. Because of medical confidentiality issues, this is not a search that local volunteers can assist us with.

Until the state birth defects surveillance system begins collecting data, it is simply not feasible to track more intensively one particular area without tracking birth defects throughout the state as a whole. Comparison data are crucial in the field of epidemiology.

Comment # 72: "At least one of the studies you cited on p. 25- Willis 1994- is seriously flawed. Also, it is not enough to focus on exposures to HTO. What about exposures to organically bound tritium (OBT)? The risk assessments you cited do not take into account the full range of possible routes for the ingestion of tritium. Please read and cite the work of T. Straum 'Health Risks from Exposure to Tritium' UCRL-LR-105088, Lawrence Livermore Laboratory, Livermore, CA (1991)."

Comment # 73: "I hope that the DPH will indeed study the potential for exposure to tritium, both HTO and OBT, in the Deerfield River Valley and that the study will be exhaustive rather than superficial."

Comment # 74: "We request that MDPH initiate a realistic risk assessment for organically bound tritium using calculations based on Straum and Cindy Folkers or other experts in the field of tritium research."

Comment # 75: "Therefore, in order to assess how much tritium from the Deerfield River evaporated as HTO, the area, depth and duration of water storage of reservoirs downriver of the initial contamination site at Rowe must be determined, or at least estimated using proper flow formulas."

Comment # 76: "Also omitted from the analysis was any valid study of organically bound tritium or dioxin. No in depth examination of contaminants or their pathways was examined. The contaminants the DRV health committee repeatedly requested the MDPH to study are organically bound tritium, dioxin, petro-chemicals, and heavy metals. The Committee continues to recommend an in-depth investigation of these dangerous substances."

Comment # 77: "Neither of the risk assessments in this section use Tore Straum's risk coefficient, nor do they address the increased risk from organically bound tritium."

Comment # 78: "However, neither risk study cited by the DPH addressed the issue of human exposure through intermediary biological pathways, i.e. milk or vegetables. MacIntosh and Willis only include inhalation, ingestion, or dermal absorption of tritium gas or HTO directly."

Comment # 79: "Since this report is only a rough draft, I think that the conclusions and recommendations will need to be rewritten to reflect a course of action that includes environmental investigation."

Comment # 80: "First, I recommend testing of the groundwater for presence of not just tritium, but other compounds such as dioxins, PCB's and heavy metals...Second, find information on the number, dimensions, flow rate and use frequency of the many holding basins in the valley. Reservoirs in Vermont clearly affect the river patterns in Massachusetts including total amount of available river water at various times. But the pollutants were not introduced until the river runs past the VT/MA border. Using reservoir data, possible total HTO evaporation can be estimated. Third, evaporation of HTO directly from the flowing river should be estimated as well as aerosolization from water flowing over the plethora of dams which cause bubbling and spraying as it travels."

Comment # 81: "In addition to groundwater sampling, plants, especially tubers and trees, need to be tested for OBT and HTO."

Comment # 82: "In conclusion, I urge you to do a fate-based contaminant transport study for both air and water routes. This involves analytically looking at how tritium could potentially be transported and making predictions of tritium concentrations in air, water and vegetation surrounding the DRV."

Comment # 83: "We need a land use history followed by a sampling of soil, water, and vegetation and a groundwater study."

Comment # 84: "Given the results of the study the MDPH should investigate the health situation in the DRV. The investigation should include tree ring analysis and well sampling. Also, check

back on the well testing that was already done. Was tritium found even if other forms of radiation weren't?"

Comment # 85: "Based on the finding of no spatial or temporal clusters, the report concludes that there is no need for environmental investigation. Your recommendations omit investigations of environmental factors and focus solely on further investigation of individual case histories. The Health Committee believes it is essential to learn more about the environmental contaminants affecting our health. Without thorough environmental investigation by MDPH, our health problems can not be seriously addressed. Given the information provided by Cindy Folkers considering the contamination of the ground water by river contaminants and recharging, it is important to include Greenfield and Colrain in the study since the potential exist that these towns as well as Whitingham, VT were effected by synergistic discharges into the Deerfield River by Yankee Atomic and Deerfield Specialty. A thorough investigation of contaminants and their effluent pathways should be undertaken. This would include:

- the investigation of ground water recharging from the river
- an examination of the ingestion pathways organically bound tritium from the Yankee Rowe reactor and from Deerfield Specialty (In operation since the 1930's using chlorine bleaching) less than a mile downstream from the reactor in Monroe Bridge.
- an examination of the ingestion pathways for dioxin from railroad spraying that parallels the Deerfield River through the valley.
- an examination of the ingestion pathways for heavy metals released as a by-product of hydro-electric power.
- Pesticides from local farms and apple orchards on Rt. 112
- Petrochemical exposure from old gasoline station on Rt. 112
- Land-fill on Rt. 112
- Ammunitions range located on Yankee Atomic property for security guards along the Deerfield River and a range on Rt. 112
- a determination of water sources for Greenfield and Deerfield.
- well testing before the half life of all these contaminants is reached
- a tree ring analysis of old growth trees along the river to ascertain emissions of tritium and dioxin.
- land use history for the 13 towns including proximity to a cemetery."

Response: This Health Consultation was intended to be an analysis of cancer incidence and DS prevalence in the DRV area, with some limited discussions of available environmental data. As such, the MDPH does not confirm or dispute the validity of the exposure assessments conducted (MacIntosh 1993, Willis 1994). It should be noted, however, that although Willis and MacIntosh each used different approaches to calculate the estimated population dose from airborne tritium, they both reach approximately the same conclusion, that the doses from nature were overwhelmingly larger than the doses from tritium from Yankee Rowe (Willis 1994).

As to conducting an investigation for chemical contamination of the DRV area, our understanding at the beginning of this project was that the major focus of concern has been related to radiological hazards, specifically Yankee Rowe. The choice of cancer types in this investigation was based primarily on evaluating those organs or systems with known or suspected radiosensitivity, although some of these cancer types may also be associated with chemical exposures. Because our office is an assessment office and not a regulatory program, we do not conduct environmental studies of chemical contamination. Requests for this type of environmental sampling should be directed to the Massachusetts Department of Environmental Protection (MDEP) and the MDPH Radiation Control Program (RCP).

Also, the available data do not suggest that residents of the DRV experienced excessive rates of cancer between 1982 and 1992 and that for most cancer types, incidence occurred at the same rate or at a lower rate than expected based on statewide cancer rates. While a few types of

cancer did show an elevation in incidence in some communities, there was no temporal or geographic pattern that would suggest an environmental factor is generally affecting the incidence of cancer in the DRV.

Comment # 86: "As the water on the Deerfield is released over the dams, it sprays and bubbles and therefore aerosolization of HTO ought to be investigated."

Response: Based on the health data evaluated, MDPH did not observe any pattern that would suggest that the Deerfield River may be associated with an increased incidence of cancer in the surrounding communities. If such sampling were to be conducted by some other appropriate agency or group, the MDPH would be willing to review this information in relation to our evaluation of cancer incidence and DS in the DRV.

Comment # 87: "The information provided by MDPH on emissions from Deerfield Specialty, Veratec, and AF and F miss the mark. The Health Committee has requested historical data on releases from the facilities. All three historically utilized chlorine bleaching in their industrial processes. The Committee is aware that both Veratec and AF and F switched to less dioxin-generating processes. However, the Committee again request MDPH recover data from the EPA on releases of dioxin as a by-product of chlorine bleaching at these facilities, and the land application of dioxin contaminated sludge in Charlemont and Heath, MA."

Response: If any additional questions or concerns exist regarding emissions or releases from facilities in the DRV (e.g., dioxin contamination related to a specific site), those questions or concerns should be directed to the Massachusetts Department of Environmental Protection (MDEP) Western Regional Office at (413) 784-1100.

Comment # 88: "We offer this perspective on the small numbers in any valley towns which can not demonstrate statistical significance due to small population size even though there were clear increases in radiogenic cancers such as bladder, breast, and pancreas. When the population is too small for statistical purposes, the data base could be expanded into abutting towns since town boundaries are arbitrary distinctions rather than demarcating the effluent pathway."

Response: To address the limitations presented by small town populations, the BEHA also calculated cancer specific rates for all 11 towns combined (see report Table 1A). When cancer incidence is examined for any town in Massachusetts, frequently situations in which the observed number of cancer cases is greater than expected are observed. Frequently, situations in which the observed number of cases is less than expected are also observed. Such variation is not unusual, which is one of the reasons that statistical tests are conducted to determine whether the observed differences may be due to chance or are not likely to be due to chance. For example, the Health Consultation contained many calculations of expected versus observed numbers of cancer, and for two-thirds of these calculations, the observed number of cases was less than expected.

The sensitivity of the breast to the carcinogenic effects of ionizing radiation have been demonstrated in numerous studies (BEIR V, p. 253). The pancreas, however, appear to be relatively insensitive to radiation carcinogenesis (BEIR V, p. 334). No literature was located regarding bladder carcinogenesis and ionizing radiation, presumably because the bladder is relatively insensitive to radiation carcinogenesis, as well.

The study area was selected for evaluation based on concerns raised by the CAN. Ashfield and ten other towns were selected because the CAN believed these to be the areas that have the greatest opportunity for exposure to emissions from the Yankee Atomic power plant.

In reference to demarcating the effluent pathway, the report did not undertake this analysis. The BEHA did describe the geographic location of cancer cases in relation to the CAN boundaries that they felt might correspond to an effluent pathway (see page 15).

Comment # 89: "A land use history accompanied by a sampling of soil, water, and vegetation, and a ground water study is required. During our meeting with CDC, MDPH committed their support for writing grants for further environmental investigation. This would involve working with other agencies such as USGS."

Response: The MDPH supports environmental investigations where such investigations are indicated. However, based on the cancer incidence data evaluated, the MDPH believes that further environmental investigations are not warranted in the DRV. It is possible that information collected as part of the DS follow-up may yield clues that can be considered in terms of environmental sampling.

Comment # 90: "A comprehensive health study is needed to investigate the epidemic of disease in our community. The Committee believes that a phase III investigation is warranted for both the cancer epidemic and the Downs syndrome. We request a household study be undertaken rather than a limited investigation of specific cancers since the problems encompass birth defects, an array of immune deficiency disease such as Hoshimotos, hepatitis C, thyroid disease, neurological disorders, and Lupus in addition to cancer."

Comment # 91: "Community groups should receive guidance on pitfalls to avoid in conducting their own investigations in environmental health surveillance. The guidance should emphasize the importance of starting with well-founded assessments of exposure and with plausible etiologic hypotheses. In addition, the guidance should stress the importance of documenting all combinations of health outcomes, town groupings, time periods, and other variables that are examined when wide-ranging searches are undertaken for possible problems in the absence of documented exposure gradients and plausible hypotheses of their effects."

Comment # 92: "We need a comprehensive health survey."

Response: Based on available data, the MDPH did not observe an epidemic of cancer in the DRV. In fact, the rates for the majority of cancers occurred at or below expected rates. During 1982-1992, in the DRV overall (see Table 1), SIRs for 6 cancer types were less than expected, SIRs for 2 cancer types were more than expected, and for the remaining cancer types an SIR was not calculated because fewer than five cases were observed. None of the SIRs were statistically significant and the elevations observed were based on an increase of 1 to 4 cases. For certain cancers for which an elevation was observed, the BEHA has conducted follow-up work to provide further information about the incidence of these cancers.

There was a statistically significant elevation in the prevalence of DS during 1980-1990. As previously indicated, if the families of children with DS request, then the MDPH will coordinate with CDC to conduct further evaluation of these cases (e.g., family interviews).

The MDPH does not generally believe that the application of a community survey to assess the types of illness of concern will yield useful information for a number of reasons. Self-reports of illnesses are often inadequate or inaccurate without a systematic method of case registration. Perhaps of greater importance is that the confidentiality of individual patient information may preclude the collection of accurate health information. It has been the experience of the MDPH that people are more likely to share personal and/or medical information with researchers who can protect the confidentiality of such information under Massachusetts General Laws.

Also, comparison data are crucial in the field of epidemiology. With the exception of cancer and certain birth defects, there is little or no comparison data available for other illnesses. Lack of comparison data makes it difficult to determine if an illness is occurring at a higher or lower than expected rate.

There are a number of other difficulties with health surveys that preclude meaningful results or interpretation of this information. For example, a major concern in this type of survey research is the occurrence of bias in participant's responses. Participants may report information which varies in a systematic way from the actual answer to a particular question. This occurs when subjects respond to a question while considering information which might not be pertinent to that question. This is of particular concern in the use of open ended questions. If such misconsiderations occur among a frequent number of participants, the results may provide an incorrect perception of characteristics in the population that the question was designed to elicit. In fact in some cases this can result in masking an association.

While such limitations are noted, the MDPH encourages residents of the DRV to work with your local health department or an appropriate epidemiological consultant if you decide to pursue this type of activity.

Comment # 93: "How peculiar that of all the conclusions in the MacIntosh risk assessment, the one conclusion not recognized in your report, stated "This analysis contains a number of simplifying assumptions which should be examined for their relevance and applicability. Specifically, an investigation should be undertaken of the potential for some of the tritium to be present in an organic molecule rather than solely as HTO. In addition, the effect of river rapids and falls on HTO evaporation, and possibly organically bound tritium aerosolization, should be researched."

Response: This is not a conclusion of MacIntosh, et al 1993, but a recommendation and suggestion for follow-up research. The four conclusions of MacIntosh, et al 1993, are stated verbatim on page 19 of the Health Consultation.

Comment # 94: "It is my understanding that some wells were tested by EPA and that tritium was detected. However its presence was not reflected in your 1997 report where you state "None of the samples detected positive result for the presence of gamma, gross alpha, or tritium." I would like to request a copy of that entire sampling report and recommend that you change your current health study to state that tritium was present in the wells or that you define what you mean by "positive result." Since three of the samples "were positive for gross beta radionuclides", I recommend you tell us which radionuclides were present."

Response: MDPH is not aware of any wells in the DRV recently tested by the EPA in which tritium was detected. Data presented in our health consultation pertained to drinking water samples collected from six residences located in the towns of Charlemont and Buckland. The sampling and locations were conducted at the request of the CAN and do not represent a comprehensive environmental sampling of the area. The MDPH Radiation Control Program conducted this sampling in December 1992, and performed analysis for gross alpha, gross beta, gamma spectroscopy and tritium. In addition, complete copies of the testing results were provided to the CAN.

The MDPH/RCP has two criteria that define a statistically positive result. First, the result must be greater than 3 times the error value of the laboratory instrument/method. The error value of an instrument defines the range within which the result is likely to exist. This is very similar to the 95% Confidence Interval used for the SIR calculations of the health statistics. Second and more importantly, the result must be greater than the instrument/method detection limit. The detection

limit is the minimum concentration that can be accurately and precisely measured by the laboratory and specified in the quality assurance plan.

It is important to understand that all drinking water supplies contain some level of radioactivity. The source of this radioactivity may be natural or man made. Drinking water supplies are sampled for the presence of radioactive materials in order to assess the dose received by an individual from the ingestion of the radioactive materials. The first level of testing for radionuclides in drinking water is a screening analysis. This screening analysis evaluates the level of gross alpha and gross beta emitting nuclides in the drinking water sample, but does not include testing for specific radionuclides. According to MDPH/RCP, if an analysis of the drinking water sample results in a gross alpha level of less than 5 picoCuries per liter (pCi/L) and a gross beta level of less than 50 pCi/L, then no additional testing of the drinking water sample is required. The methods used by the MDPH/RCP to analyze radioactivity in drinking water are acceptable to the USEPA and the MDEP.

In the DRV, six samples were analyzed for radionuclides. Of the six samples, five were taken from residential properties in Charlemont, and one was taken from a residential property in Buckland. None of the six sample analyses exceeded the regulatory limits for the individual analyses performed on each sample. In addition, neither the gamma spectroscopy analyses, the gross alpha analyses, nor the tritium analyses resulted in a statistically positive result.

Only the gross beta analyses showed a statistically positive result. One gross beta sample measured 3.4 pCi/L. This result was greater than the minimum detection limit of 3.0 pCi/L. This result is also, however, well below the regulatory limit of 50 pCi/L.

Comment # 95: "I recommend you put the total population which you are researching in this report since the reader has no total population reference point."

Response: The population figures used in this analysis were interpolated based on 1980 and 1990 U. S. census data for each town (see page 2). The 1980 population for all 11 DRV towns combined was approximately 14,210 of which 7,043 were males and 7,167 were females. The 1990 population for all 11 DRV towns combined was approximately 15,719 of which 7,783 were males and 7,936 were females. The total interpolated (1987) population (11 DRV towns) used for analysis in this report was 15,278; of which 7,565 were males and 7,713 were females. These data are presented in Table A-9.

Comment # 96: "DPH should assess prostate cancer since two UK Atomic Energy Authority studies show that increase in prostate cancer death might be related to tritium exposure. Moreover, in a study conducted by Yamamoto and referenced in my risk assessment, researchers found that malignant lymphomas showed dose-response for tritium exposures. Further, as the dose decreased, not only did the lymphomas decrease, but solid tumors increased. All the animals in Yamamoto's study were female, therefore no male comparison was possible. DPH registered an increase in lymphomas, especially in females."

Response: First, the focus of the DRV Health Consultation was to answer specific questions regarding citizen reported increased cancer incidence and DS prevalence in the DRV based on concerns related to Yankee Rowe. Massachusetts Cancer Registry data for the years 1987-1994 indicates that the incidence of prostate cancer in the DRV towns occurred statistically significantly less often than expected when compared to statewide incidence (62 observed versus 83 expected). These results are presented in Table A-9.

In addition, although females in the town of Deerfield did experience a statistically significant increase in the incidence of NHL, available risk factor information does not suggest that a causal relationship exists between tritium exposure and the development of NHL.

Lastly, the Yamamoto study referenced (*Assessment of Cancer Risk to Communities of Deerfield River Valley, MA, from Exposure to Milk Containing Tritium*. Yamamoto, O., Yokoro, K., et al. Carcinogenic Effect of Tritiated Water (HTO) in Mice in Comparison with Those of Fission Neutrons and Gamma Rays. Tritium Radiobiology and Health Physics, Proceedings of the Third Japan-US Workshop 1989) did not find a dose-response relationship between lymphomas and tritium exposures. The results of the study showed that total-body irradiation of neutron and gamma rays and an injection of HTO beta rays were not found to cause leukemia in the mouse strain used in this experiment. Page 225 of the Yamamoto study specifically states that, "The frequency of leukemia development in the three irradiated groups was low... and comparable to that in non-irradiated controls".

Comment # 97: "DPH should state clearly why the entire state of Massachusetts qualifies as a "normal population", even if using a state is accepted practice. Considering that the state as a whole has a higher breast cancer rate than other states and the state received pollution from at least three nuclear power reactors, many TRI and 21E sites as well as it's share of Superfund areas, using state data would make cancer incidence in DRV seem low compared to "background incidence."

Response: The state of Massachusetts was selected as the 'normal' population for three reasons. First, the state represents a large population, and therefore a stable population base to derive statistics to be used for comparison. Second, because the Massachusetts Cancer Registry collects statewide data, using the state as a comparison to the DRV maintains the greatest degree of reliability and validity. Finally, as stated, it is the accepted practice. Using other state databases (or cancer registries) may produce a higher SIR but weakens the validity of the comparison values (SIRs) because of potential differences between states in population structure, prevalence of risk factors and in reporting methods and accuracy.

Comment # 98: "What happens if you compare our incidences of cancer with comparably rural (but not dominated by agribusiness) areas which don't have a nuclear plant pumping tritium into the river, or factories adding some dioxin for good measure?"

Response: The incidences of cancer could be greater, less, or equal, depending on the other underlying risk factors, differences in population age structure, and other characteristics of the population in a comparably rural region. The BEHA used the state of Massachusetts for a comparison because it represents a large population with stable rates and is the most appropriate comparison base available.

Comment # 99: "DPH states that 'A total of 159 cases (approximately 57% of the mapped cases) were located outside of the CAN boundary.' It is my understanding that the Citizens' Awareness Network drew these lines to mimic valley wall boundaries and, further, that the DPH based cancer case position on residence, not place of employment. Current place of employment must be considered. More importantly, DPH should attempt to discern place of employment and residence at the time of greatest potential effluent exposure: the years between 1961 and 1972-73 with the understanding that pathways of exposure must be fully assessed. During these years, the nuclear station released the most tritium effluent due to faulty fuel rods which were replaced in the early 1970's."

Response: The available data from the Massachusetts Cancer Registry only list occupational fields or type and not the employers' address. Hence, no information is available for mapping cases by place of employment. However, for some cancers (NHL and multiple myeloma) follow-up research will attempt to determine residential and occupational histories. This will help to determine if length of residence is plausibly related to environmental exposures, as well as to determine plausible occupational risk factors for these diseases.

In addition, based on our review of available surveillance data (i.e., Massachusetts Cancer Registry Data 1987-1992) it does not appear that residents of the DRV experienced excessive rates of cancer during the period 1987-1992. Further, research and review of residence and employment (i.e., during 1961-1972) of all cancers is not warranted based on this review of surveillance data.

Comment # 100: "Please refrain from comparing any additional human-made radiation release to "background". First of all, determining exactly what background is (or should be) is difficult since most "background" measurements were taken after our explosion of atomic bombs within our own atmosphere. Second, saying something is "below background" radiation levels might lead the public to believe it is safe when it is most assuredly not. While a release may be "below background", it is in addition to background radiation exposure to humans, therefore, it is compounding risk, not matter how "little" is added. Again, this is an industry attempt to make a comparison which serves no purpose and acts to mislead. In fact, the EPA recognizes no safe level of radiation."

Response: Use of the term 'background' was not intended to imply safe but rather that there is radiation that is considered "background" and occurs from many sources. Generally, in a given area (e.g., Massachusetts, New England) everyone is exposed to some level of background radiation. Measuring health outcomes due to potential exposure is only useful if there is an exposure to a certain group above the background levels that other groups may be exposed to. Thus, if there are differences in exposures between the two groups, one might see differences in health outcomes that, with other factors being considered, could potentially be related to the exposure of interest. Based on the two risk assessments (MacIntosh 1993, Willis 1994) there is no clear indication that DRV residents received more exposure to radiation than other residents in Massachusetts. In addition, when compared with the state, cancer incidence in the DRV was approximately equal to or less than expected, overall.

Comment # 101: "Your report concludes (on page 28) that "it is unlikely that tritium exposures to DRV residents would result in an increase in the occurrence of cancer or Down Syndrome." We agree with this conclusion and feel that it ought to be highlighted in your report. Your conclusion makes sense because doses from tritium are several orders of magnitude below natural background. We know this because we have monitored our releases and published those releases for 37 years and have also collected and analyzed 35,000 environmental samples. The States own environmental sampling of water "did not detect the presence of gamma, gross alpha, or tritium" (page 25). This, plus the fact that the Down Syndrome cases were, on average, 12.5 miles from the plant, supports the conclusion that tritium exposures are an unlikely cause. Yankee also wishes to note that we are on record as supporting the establishment and implementation of a Statewide birth defects registry (see Dr. S.P. Schultz letter to Barrett, 3/18/94). The cancer analyses demonstrate a remarkably favorable pattern of cancer incidence rates in the 11 town study area. Residents of the towns should be greatly reassured by these results. The remarkable pattern of lower than expected cancer incidence rates should be highlighted in the report. This news should be appropriately reassuring to all concerned residents of the Deerfield River Valley."

Response: The BEHA feels that this information has been sufficiently discussed in the Health Consultation.

Comment # 102: "Yankee has asked Dr. Poole of Boston University to provide detailed comments directly to you. Dr. Poole's analysis shows that if all Valley residents had the same chance of cancer as the rest of the State, then 323.5 SIRs would have been elevated. Your report found only 267 which is 56 less than expected. This result is statistically significant. It should be highlighted and should provide assurance to the residents."

Response: The Health Consultation contained many calculations of expected versus observed numbers of cancers, and for over two-thirds of these calculations, the observed number of cases was less than expected. These findings are consistent with Dr. Poole's analysis.

Comment # 103: "In the absence of serious collaborative partnerships in research, outside scientific investigations will not be trusted or accepted by the citizens that requested these studies in the first place. I urge you to respond to environmental health concerns in the Deerfield River Valley by working closely with citizens to utilize local knowledge and talent in continuing investigations. Such a strategy holds the promise of not only better science, but better trust between scientists and the public."

Response: The MDPH has a strong commitment to working with community members. Some of the information contained in our report was collected and provided to the MDPH by community members (i.e., the CAN). The MDPH had numerous discussions with the CAN and received their input in the planning and conduct of this evaluation.

Comment # 104: "The report shows that the prevalence at birth of Down syndrome was elevated in the study area in the years 1980-1990. Eight children were born with Down syndrome when two or three would have been expected on the basis of data from California. For reasons adequately summarized in the report, it is extremely implausible that pollution from Yankee Rowe had anything whatsoever to do with this excess. The only plausible hypotheses of which I am aware are as follows:

a. The result is well within the range of ordinary variation in the frequency of health outcomes, but appears impressive because it is presented in isolation from the extensive review of town-level health statistics over several years that led to the selection of Down syndrome and the grouping of these 11 towns in particular as the study area. To test this hypothesis, it would be necessary to place the result for Down syndrome in these 11 towns into the context of all the health outcomes and all the alternative groupings of towns examined during that review. In such a process, it often is possible to piece the information together in a way that seems alarming if viewed apart from the full context. This is a very natural trap to fall into, even when the process of prior review and selection is conducted with the best of intentions.

b. Among the parents in the study area over the 11-year period, a handful more than expected from experience in California did not utilize amniocentesis services, received inaccurately negative test results, or chose to continue their pregnancies when the testing detected the presence of Down syndrome."

Response: MDPH acknowledges these hypotheses as possibly playing some role in the elevated rate of DS. However, the MDPH did not obtain case specific information on the mother's use of pre-natal screening services and therefore cannot evaluate how this may have impacted the rate of DS in the DRV in either a positive or negative direction. However, a reduced utilization of amniocentesis in the DRV is partially supported by data indicating that during 1992, the percentage of mothers who did not receive prenatal care during the first three months of their pregnancy was higher in the DRV area (15%) than in Massachusetts (13%) (Health Status Indicators, Community Health Network Areas, 1994).

Comment # 105: "There is no good reason for the Department to carry out its plans to conduct further reviews of non-Hodgkin's lymphoma among females in Deerfield or of multiple myeloma in the 11 towns as a group. These reviews would be of nine and 11 cases, respectively, and would not be expected to produce any information of public-health or scientific value."

Response: The MDPH will carry out its plans to conduct further reviews because we believe the information may help us learn more about the incidence of cancers in the DRV towns.

Comment # 106: "The Department's proposal to investigate further Down syndrome in the Deerfield River Valley should not be pursued without a firm commitment to explore fully the hypotheses concerning utilization and accuracy of amniocentesis testing and decisions concerning the continuation of pregnancy based on the results of such testing. These are extremely sensitive issues, personally and politically. Nevertheless, if an investigation were to sidestep them, it would fail to address the leading possible explanation and therefore would not be worth conducting."

Response: If the families of children with DS request follow-up, then this comment will be considered and discussed with the Centers for Disease Control.

Comment # 107: "While the individual statistics appear to be correct I believe that the public can easily be misled by the so called 'significance' of the test due to the multiple comparisons made. While the significance level of any one test chosen a priori to the study is accurately reflected in the traditional 95% confidence level, it is inappropriate to screen and select out the significant ones for comment when many such test are made. After all, even with random 'senseless' data, one would expect to see 'significant' results at the 95% confidence level in about 1 in 20 cases...While scientist may recognize this issue and realize the true level of significance is much less when multiple test are conducted, laypersons and newspaper summaries may pick out a significant result from the tables and come to an incorrect conclusion, despite what is stated in the conclusions section of your report. Perhaps a multiple comparisons test could be conducted such as Scheffe's test. I believe the reporting of many multiple comparisons as significant is the most serious issue that needs to be addressed in your report."

Comment # 108: "The Department should consider implementing improved statistical methods for making the hundreds and thousands of comparisons involved in environmental health surveillance projects such as this. Hierarchical modeling techniques such as empirical-Bayes or semi-Bayes analysis has been shown to reduce overall error substantially in applications exactly like this one. Such methods can be implemented without too much difficulty."

Comment # 109: "As a prelude or adjunct to the methods described above, the Department should consider using simulation methods such as those employed in this review to provide appropriate contexts for interpreting results from analyses in environmental health surveillance."

Comment # 110: "The hierarchical modeling and simulation methods would obviate the perceived need for a decision rule to conduct formal comparisons only when the observed number of cases or deaths exceeds a minimum value (four in this report). If the Department still feels the need for such a rule, it should be based on the expected number of cases, not on the observed number. Then the formal comparisons will be those for which the results are most statistically stable."

Comment # 111: "Separate analyses should not be conducted in the subset of towns that experienced at least one occurrence of a selected outcome. This procedure is biased toward overestimating associations."

Response: The Department understands issues related to conducting multiple statistical tests. For this reason, the BEHA always carefully evaluate the data in total, (e.g., consistency across time, geographic location, and plausibility of relationships). Decisions about possible follow-up or the importance of findings is based on the overall assessment of the data.

Comment # 112: "One additional minor point involves your reported rate of DS per 1000 births. If the study was directed at 11 towns the results should be reported for 11 towns. Why was another statistic reported for the 5 towns with DS cases? This would seem to inflate the rate. One could just as well report the rate for the 0.25 mile square area in Buckland where 3 cases were

reported. I'm sure the rate would be very high, but such selected reporting is not justified or explained in your report."

Comment # 113: "The analysis confined to the five towns in which Down syndrome cases were born is inappropriate and should be deleted. It is clearly biased toward overstating associations. If extended (to the census tract, block, household, etc.), it ultimately would be guaranteed to produced prevalence odds ratios approaching infinity. As with the cancer analyses, appropriate methods can be used to provide the necessary context and to reduce the probability of error due to small numbers. If a criterion for defining a subset of the towns is desired nonetheless, the criterion should be based on the expected number of cases, not on the observed number."

Response: MDPH agrees that the analysis confined to the five towns in which Down syndrome cases were born is biased toward an elevated prevalence. The five town prevalence was calculated to provide a worst case scenario. It is the practice of public health agencies to use this approach in an effort to ensure to the extent possible that a potentially important finding is not overlooked.

Comment # 114: "It is inaccurate to state that the results "...did not generally indicate that maternal age was a significant risk factor among these cases" (page 22) and that "maternal age did not appear to be a significant risk factor among the children with Down syndrome in this area" (page 27). In fact, prevalence computable from the second and third columns of Tables 15 and 16 show that maternal age was strongly related to the prevalence of Down syndrome at birth in the 11 towns, as it has been in virtually every population ever studied. What the analysis showed was that maternal age was not an important confounder of the comparison between the 11 towns and California, the reference population. From the results provided (specifically, the slight increase in the expected number from 2.21 to 2.46 when maternal age was controlled), we can infer that the absence of appreciable confounding by this strong risk factor was due to the fact that the maternal age distribution in the 11 towns was shifted only slightly toward older ages in comparison with the California distribution."

Response: Discussions of maternal age as a potential risk factor or confounder have been clarified in the Health Consultation.

Comment # 115: "Why are only the near significant test of increased cancer noted while the near significant tests of decreased cancer incidence are not discussed? For example, in the Conclusions section it is noted that "Elevations in multiple myeloma...were not statistically significant.", but the decrease in lung cancer compared to expected is also nearly significant (Table 1A). The fact that lung cancer is one of the primary targets for ionizing radiation which was the focus point of the entire study. Decreases should be given the same scrutiny as increases in an unbiased study."

Response: For the purposes of evaluating all data for possible public health follow-up, the MDPH was most interested in those health outcomes that may be significantly or nearly significantly elevated in order to further evaluate possible reasons for these elevations. The MDPH acknowledges that we could also discuss nearly statistically significant decreases.

Comment # 116: "Perhaps a summary statement could be included that overall there is less cancer in the valley than expected (323 cases vs. the expected 348.8 from Table 1A)."

Response: MDPH has stated that overall, the DRV is not experiencing excessive rates of cancer. The BEHA typically does not combine and compare all cancer types because it obscures potentially important variability among individual cancer types, which may have different etiologies (causes), and risk factors.

Comment # 117: "It would also appear that many significant decreases in cancer would not be reported by your convention to report NC (Not Calculated) when cases are low. Some of this is discussed in the Limitations sections, but frankly the public does not read such sections. I suggest you add some discussion to the Conclusions section which restates the limitations and says to the effect "...the only conclusions which can be made are the following...". Otherwise the public will tend to grab one or two selected 'significant' statistics and say this is the tip of the iceberg."

Response: Understanding and comprehending the limitations of a study is important when interpreting its results. For this reason, the Limitations section is located directly before the Conclusions section in our report. The DRV Health Consultation is specifically formatted to communicate information that the general public will be able to use and understand. To facilitate this, the Conclusions section is written in simple direct statements, which highlight the most important public health issues derived. Conclusions are meant to be explicit and unambiguous, stating concisely the findings of the Health Consultation. The Department does not believe that re-stating the study limitations in the Conclusions section will help to further clarify or communicate information to the public.

Comment # 118: "The Conclusions section appears to give equal weight to the overall conclusions in the first two bullets as it does to the many individual significant statistical results by cancer type and town in the remaining bullets. I suggest you separate general conclusions from specific conclusions and again, discuss what is the true level of significance given the number of test."

Response: The MDPH has clarified this point in the Conclusions section of the Health Consultation.

Comment # 119: "In the recommendation section perhaps you could include age of first childbirth as a potential cofactor to be investigated in breast cancer?"

Response: The recommended follow-up work on breast cancer in Shelburne will continue to rely on existing surveillance data (MCR data). Although personal factors and information such as the age of first childbirth for individual women diagnosed with breast cancer is not available in this database, we are able to assess this information in the general population overall. Please refer to Appendix C: Shelburne Breast Cancer Follow-up for further discussion.

Comment # 120: "One final note on the boundaries of the Deerfield River Valley. The boundary defined by the CAN does not correspond to the watershed boundary as indicated on official maps. For example, the boundary of the Deerfield watershed is much larger as shown on the map "Massachusetts River Basins" produced by the Department of Environmental Management in 1985. It should be made clear in the report that the boundary defined by CAN is not the watershed boundary but is an area within the watershed."

Response: It is correct that the Deerfield watershed is larger than the CAN boundaries. However, the MDPH has not defined the DRV area as the watershed area. We have only used the boundaries provided by the CAN to address their concerns. Also, please note that the CAN defined their boundaries based in an attempt to address concerns about exposure to air contaminants, not water.

Comment # 121: "With regard to the two 21E sites located in Conway center as of 1995-more recent information should indicate that one or both of them require no further remedial response actions, it seems to me-one is probably the slight leak from the old underground heating oil tank at the Conway Town Hall which has been officially remediated for a year or more I believe."

Response: In 1997 the MDPH reviewed information on 21E sites located in the 11 DRV towns and listed by the Massachusetts Department of Environmental Protection. The available information indicates that the Conway Town Hall is currently listed as a confirmed disposal site whose status is shown as "Response Action Outcome". This classification is applied to sites at which there is No Significant Risk as defined by the Massachusetts Contingency Plan (MCP) (310 CMR 40.1000). The second 21E site, also located in Conway Center, has been listed as a remedial site requiring no further action.

Comment # 122: " Since the increase in Down Syndrome seems to have peaked in the 1982-1992 period. I think it is important to follow the cancer incidence for the next 8-10 years since it can take several years for cancer to manifest clinically."

Response: As stated in the report, the MDPH will continue to monitor cancer incidence in the DRV through the Massachusetts Cancer Registry.

Comment # 123: "At the public meeting you stated that it was not part of this first study to investigate the causes of the increased incidences of cancer and DS you found and yet you felt entitled to draw conclusions about the dose of tritium received by residents and its effects."

Comment # 124: "In the meantime I strongly urge you not to draw conclusions about matters you do not even claim to have investigated in your report. As you yourselves say, "This investigation is descriptive in nature." Your report should reflect this fact. It should state very clearly that you are not ruling out environmental causes for the increases in cancer and DS you found here."

Response: Descriptive evaluations can provide information on patterns and trends that may suggest that a common etiology is possible or may suggest an excess of well established risk factors in a certain area. It is important to understand that the DRV did not experience an elevation in cancer. The MDPH can not determine whether exposure to tritium or any other factor related to the development of cancer (e.g. diet, genetics, etc) caused an individual's cancer.

The MDPH will modify the report to state that the environment (i.e., exposure to tritium) has not been ruled out as a potential factor in cancer and birth defects in residents of the DRV. However, based on health risk assessments conducted by other researchers and the available data reviewed in this report, it seems unlikely that tritium exposures to DRV residents would have resulted in an increase in the occurrence of cancer or Down Syndrome.

B. Review of Residential History and Risk Factor Information for Non-Hodgkin's Lymphoma and Multiple Myeloma in the Deerfield River Valley, MA

Background

In February 1997, the Community Assessment Unit of the Massachusetts Department of Public Health, Bureau of Environmental Health Assessment (MDPH, BEHA) conducted an evaluation of cancer incidence and Down syndrome prevalence for 11 towns in the Deerfield River Valley (DRV). The health consultation concluded that the available data did not suggest that residents of the DRV experienced excessive rates of cancer during the period 1982-1992 (MDPH 1997). The majority of cancer types evaluated occurred at the same rate or at a lower rate than would have been expected based on statewide cancer incidence. Further, in the 11 towns evaluated, no unusual temporal or geographic patterns were observed which would suggest that a single factor, environmental or non-environmental was related to the incidence of cancer in this area.

However, as a result of these analyses, elevations were noted in specific cancer types.

Non-Hodgkin's lymphoma (NHL) was statistically significantly elevated among females in the town of Deerfield. This elevation was based on an excess of approximately five cases. The elevation was mostly the result of a greater number of NHL cases that occurred during the later portion (1987-1992) of the 11-year period evaluated.

The incidence of multiple myeloma was not statistically significantly elevated in any of the 11 DRV towns evaluated during 1982-1992, and the individual cases were widely spread geographically throughout the region. However, an elevation in multiple myeloma was noted in the 11 DRV towns overall. Although, the incidence of this cancer was not statistically elevated, a consistent elevation in multiple myeloma was noted for both males and females in the 11 towns combined, particularly during the later portion of the time period (1987-1992).

A statistically significant elevation of breast cancer was observed in the town of Shelburne. In Shelburne, the rate of breast cancer appears to have increased over time and was most pronounced during the later portion of the 11-year time period 1987-1992.

Based on these findings, several recommendations were made in the health consultation. As a follow-up activity, the MDPH, BEHA completed an in-depth analysis of breast cancer incidence in Shelburne. A separate report that describes the findings of this analysis is attached as Appendix C. The MDPH also recommended further evaluation of the residential and occupational histories of individuals diagnosed with NHL and multiple myeloma during 1982-1992 in the DRV. The following sections describe the findings of residential and occupational history as well as other relevant risk factor information for NHL and multiple myeloma.

II. Discussion

For each cancer type reviewed here, available information on latency (the period from exposure to an agent or substance and disease presentation), patterns of occurrence (e.g., age at diagnosis), and risk factors in the general population have been summarized. The information on individuals diagnosed during 1982-1992 with NHL and multiple myeloma in the DRV area was then compared with known information about the occurrence of risk factors for these cancer types in the general population.

A. Non-Hodgkin's Lymphoma

Lymphomas are cancers involving the cells of the lymphatic system. The majority of lymphomas involve the lymph nodes and spleen but the disease may also affect other areas within the body (ACS 1996). Non-Hodgkin's lymphoma (NHL) is a classification of all lymphomas with the exclusion of Hodgkin's disease. Thus, NHL is a mixed group of diseases that is characterized by the malignant increase in specific cells of the immune system (B or T lymphocytes). The various types of NHL are thought to represent different diseases with different causes (Scherr and Mueller 1996). NHL can occur at all ages however, the incidence of this disease generally increases with age. Among all NHL types there is a greater male to female ratio and white to black ratio (NCI 1996). In Massachusetts, the incidence of NHL among males increased by 53% from 11.5 cases per 100,000 in 1982 to 17.6 cases per 100,000 in 1992. Among Massachusetts women, the incidence of NHL increased by 22% over the 11-year period 1982-1992 (MCR 1995).

Nationally the increase in NHL incidence has been attributed to changes in case classification, better diagnostic techniques, greater exposure to causative agents, and the increasing incidence of AIDS-related lymphomas (Devesa 1995; Scherr and Mueller 1996). Although the primary factors related to the development of NHL include conditions that suppress the immune system, viral infections and certain occupational exposures, these factors are thought to account for only a portion of the increase observed in this cancer type (Scherr and Mueller 1996).

In the town of Deerfield, 11 cases of NHL occurred during 1982-1992. Approximately eight cases would have been expected in the town during this period based on the statewide incidence of this cancer. Among males, two cases occurred and among females, nine cases occurred. The incidence of NHL among females in Deerfield was statistically significantly elevated (SIR=238, 95% CI, 109-452). The median age of NHL cases in Deerfield was 65 years. In addition, the age pattern of the cases showed a trend of increasing incidence with increasing age as the majority of cases (91%) were diagnosed in the age groups 45-64 years and 65-74 years. This pattern is consistent with the known pattern of incidence of NHL. However, NHL is generally more common among men than women. In Deerfield, a greater ratio of female to male cases was observed.

NHL is more common among people who have abnormal or compromised immune systems, such as those with inherited diseases that suppress the immune system, organ transplant recipients, and individuals with autoimmune disorders (Scherr and Mueller 1996). NHL has also been reported to occur more frequently among individuals with conditions that require medical treatment resulting in suppression of the immune system, such as cancer chemotherapy. However, current evidence suggests that the development of NHL is related to suppression of the individual's immune system as a result of treatment rather than the treatment itself (Scherr and Mueller 1996).

Several viruses have been shown to play a role in the development of NHL. Among organ transplant recipients, suppression of the immune system required for acceptance of the transplant leads to a loss of control or the reactivation of viruses that have been dormant in the body (e.g., Epstein-Barr Virus (EBV) and herpesvirus infections). In addition, cancer-causing viruses are known to cause lymphoma in various animals. Therefore, it has been proposed that these types of viruses may also be associated with the development of NHL among humans without compromised immune systems (Scherr and Mueller 1996). The infection with the human T-cell leukemia/lymphoma virus (HTLV-I) is known to cause T-cell lymphoma among adults. However, although this type of virus is known to cause lymphoma, it is a relatively rare infection and most likely contributes only a small amount to the total incidence of NHL (Scherr and Mueller 1996). Since EBV infection is common among the general population and has been shown to play a role in the development of most cases of transplant and AIDS related NHL, several studies have been conducted to determine the role of EBV infection in the development of NHL in general. These

studies have shown that although viruses are causal factors for some subtypes of NHL, their role in the development of NHL as a whole may not be large (Scherr and Mueller 1996).

Some occupations have been associated with an increased risk of developing NHL, specifically occupations related to chemicals or agriculture. Farmers, herbicide and pesticide applicators, and grain workers appear to have the most increased risk (Zahm et. al. 1990, 1993; Tatham et. al. 1997). Studies conducted among agricultural workers have demonstrated increases in NHL among those using herbicides for more than 20 days per year and individuals who mix or apply herbicides. A greater incidence of NHL appears to be related specifically to exposure to the herbicide 2,4-dichlorophenoxyacetic acid (2,4-D) and organophosphate insecticides (Wigle et. al. 1990; Zahm et. al. 1990; Zahm et. al. 1993). Further studies of exposure to these chemicals and NHL incidence have shown that the increased risk is attributed to a specific impurity, 2,3,7,8-tetrachlorodibenzo-p-dioxin or 2,3,7,8-TCDD, present in these herbicides. However, reports of accidental industrial exposures to TCDD have not demonstrated an increased risk of NHL (Scherr and Mueller 1996). An elevated risk for NHL development has also been noted among fence workers, orchard workers, and meat workers.

Occupational histories were compiled for individuals diagnosed with NHL in Deerfield by reviewing resident lists for the town (Town of Deerfield 1950-1992). Review of this information for the 11 cases revealed that two individuals had possible long-term occupational exposures in agriculture (i.e., greater than 20 years). Occupational histories for six of the cases did not reveal occupations that have been associated with an increased incidence of NHL. Occupational histories for three cases were not able to be determined.

Cancer in general has a lengthy latency period that can range from 10 to 30 years and in some cases may be more than 40 or 50 years (Bang 1996, Frumkin 1995). The latency period is the period between exposure to a disease-causing agent and the appearance of manifestations of the disease (Last 1995). For the majority of tumors, the period between first exposure and appearance of the tumor is 12 to 25 years (Bang 1996). A residential history allows for determining the length of residence for individual cases in a certain area. This information can be useful in determining whether residence in a specific area could be related to the development of cancer given the latency period for that cancer. Residential histories were constructed for the 11 NHL cases from town resident lists. Among the individuals diagnosed with NHL in Deerfield during 1982-1992, approximately 55% (n=6) were long-term residents of the town (i.e., greater than 10 years) prior to diagnosis. The majority of these individuals were residents of Deerfield for greater than 20 years. Two individuals lived in Deerfield for less than five years before their diagnosis with NHL and residential histories could not be determined for three individuals. Although additional review for these three cases resulted in no further information, it is possible that these individuals lived in Deerfield for only a brief period prior to their diagnosis with NHL and were therefore not listed in the town resident lists.

In addition, epidemiological studies of long-term users of permanent hair coloring products have found an increased incidence of NHL (Zahm et. al. 1992; Scherr and Mueller 1996). However, a recent population based study found no association between the use of hair-color products and an increased risk of developing NHL. The researchers further stated that results from this study and previous studies, including experimental animal studies, provide little convincing evidence linking NHL with normal use of hair-color products (Holly et. al. 1998).

Some studies have also found a positive association with the incidence of NHL and smoking. In a recent population-based study, an increased risk was found among all NHL types and smoking (Brown et. al. 1992). However, a significant relationship was not observed as the amount of smoking increased. In contrast, a study that evaluated the history of tobacco use and deaths from NHL determined that people who had ever smoked had a two-fold increase of dying from NHL as compared to those who never smoked. Further a four-fold increase was found among the heaviest smokers (Linnet et. al. 1992). In addition, a more recent study that primarily examined

occupation and NHL risk found a significant association with high levels of cigarette smoking and all NHL types (Tatham et. al. 1997). Among the NHL cases diagnosed in Deerfield during 1982-1992, approximately 36% were current or former smokers at diagnosis. Three individuals reported that they had never smoked and smoking status was unknown for four individuals (approximately 36%).

B. Multiple Myeloma

Multiple myeloma is a cancer of the plasma cells. Plasma cells are usually found in the bone marrow and produce immunoglobins or antibodies that circulate in the blood to help in fighting disease (NCI 1996). Although the incidence and mortality of multiple myeloma have been increasing, this disease continues to be a relatively rare cancer with an obscure etiology or cause (Riedel and Pottern 1992). In the United States, multiple myeloma accounts for approximately 1% of cancers and occurs twice as often in blacks than whites (Schwartz 1997). The onset of the disease generally occurs late in life and typically, the median age of diagnosis is 69 for men and 71 for women (Riedel and Pottern 1992).

In the 11 DRV towns combined, 11 cases of multiple myeloma occurred during 1982-1992 where approximately seven cases were expected based on the statewide incidence of this cancer. Although, the incidence of multiple myeloma was not statistically significantly elevated in the DRV area, a uniform elevation in this cancer type was noted for both males and females in the 11 towns combined, particularly during the later portion of the time period (1987-1992). The median age of multiple myeloma cases in the DRV was 72 years. More male cases were observed than female cases (55%). Both the age and gender distribution of multiple myeloma cases in the DRV is consistent with the known epidemiology for this disease.

The most well established risk factors for multiple myeloma include exposure to pre-existing medical conditions, exposure to ionizing radiation, certain occupational exposures, familial occurrence, and genetic history. Pre-existing medical conditions such as monoclonal gammopathy of unknown significance (MGUS) and chronic antigenic stimulation increases a person's likelihood of developing multiple myeloma (Herrinton et. al. 1996; Riedel and Pottern 1992). MGUS is an asymptomatic, non-malignant disorder that causes production of certain components within the immune system and proliferation of plasma cells (Herrinton et. al. 1996). Because multiple myeloma affects plasma cells, the wellness of a person's immune system is of particular interest. Experimental observations and some case reports support the hypothesis that after prolonged stimulation of the immune system by repeated infection, allergic conditions, or autoimmune disease, the risk of multiple myeloma increases (ACS 1996; NCI 1996).

Exposure to ionizing radiation is perhaps the most recognized and definitive risk factor for multiple myeloma (Riedel and Pottern 1992). Increases in the incidence of multiple myeloma among atomic bomb survivors and radiologists have provided the most evidence of an association between radiation exposure and this cancer (Riedel and Pottern 1992). Workers at nuclear power plants may also be at an increased risk for multiple myeloma (NCI 1996). However, studies examining residential proximity to nuclear facilities have found no association with this cancer (Riedel and Pottern 1992).

Studies on various occupations have consistently linked multiple myeloma with agricultural occupations (Reidel and Pottern 1992). However, the actual role of occupational exposures in the development of this cancer remains unclear (Reidel and Pottern 1992). Other studies have shown associations between the risk of multiple myeloma and employment in leather tanning, rubber manufacturing, and metal industries (Riedel and Pottern 1992). Among chemical agents, some studies have reported positive associations between exposure to pesticides, engine exhaust, and paints and an increase in multiple myeloma (Herrinton 1996). However, published literature on the relationship between benzene exposure and multiple myeloma is inconclusive and does not

indicate that exposure to benzene is a risk factor for this disease (Bezabeth et. al. 1996). Review of occupational histories for the 11 individuals diagnosed with multiple myeloma in the DRV did not reveal any occupations associated with an increased risk of the disease.

Although multiple myeloma occurs in families, there is no definitive evidence to conclude that multiple myeloma is an inherited disease (Riedel and Pottern 1992). There is some evidence for a genetic predisposition for multiple myeloma (NCI 1996). Of the genetic markers examined, human leukocyte antigen (HLA), in particular, has been positively associated with an increase in developing this cancer (Reidel and Pottern 1992). Other possible risk factors that may be related to multiple myeloma include obesity (Freidman and Herrinton 1994) and low socioeconomic status (Koessel et. al. 1996).

III. Summary/Conclusions

Review of available information related to risk factors for NHL did not reveal any pattern among NHL cases in Deerfield that was not consistent with established epidemiology for this cancer. Review of available information for individual cases indicated that six of the 11 cases had personal risk factors that have been shown to be associated with an increased risk of developing NHL (i.e., occupation and smoking). Occupational histories revealed that two individuals had long-term occupations in agriculture for at least 20 years. In addition, approximately 36% of the NHL cases in Deerfield reported being a current or former smoker at the time of diagnosis. Therefore, it is likely that these factors may have played a role in the development of NHL for some individuals and that the environment alone was not a primary factor in the overall incidence of this disease.

Approximately 50% of the NHL cases in Deerfield were long-term residents of the town (i.e., greater than 10 years). While some NHL cases resided in Deerfield for more than 20 years, residential histories showed that the remainder of the case group lived in Deerfield for less than five years prior to diagnosis. Although residential histories could not be compiled for three of the NHL cases in Deerfield, it is likely that these individuals resided in Deerfield for only a short period prior to diagnosis and therefore were not listed in the town's resident lists. Given the latency period for development of cancer and additional information about the cases regarding other risk factors, it is likely that residence alone is not a primary factor in the development of NHL in this area.

The incidence pattern (i.e., age and gender ratio) of multiple myeloma cases in the DRV was consistent with the established epidemiology for this cancer. However, evaluation of this cancer type presents a serious challenge because other than pre-existing medical conditions and certain occupational exposures, the cause of multiple myeloma remains largely unknown. Moreover, occupational histories for multiple myeloma cases diagnosed in the DRV did not reveal any occupations among the cases that have been suggested as related to an increased risk of developing this cancer.

It is difficult to draw any definitive conclusions based on the available information about cases of NHL and particularly multiple myeloma in the DRV. The information reviewed in this assessment is descriptive and therefore somewhat limited in nature. For example, although occupational and smoking histories were available for a number of cases, the information was limited to job title and smoking status reported as current or former smoker. Furthermore, no information was available regarding specific chemical or pesticide exposures, the duration and/or the amount of possible exposure. In addition, the number of cases evaluated was relatively small and information was incomplete or unknown for some of these cases. Therefore, this evaluation can not determine any causal relationship between risk factors and the development of cancer types investigated in the DRV but can assess the possibility that some risk factors may have played a role in the development of cancer in this area.

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C. Evaluation of Female Breast Cancer Incidence in Shelburne, MA 1982-1994

I. BACKGROUND

In December 1993, the Massachusetts Cancer Registry (MCR), a division of the Bureau of Health Statistics, Research and Evaluation within the Massachusetts Department of Public Health (MDPH), published the report, *Cancer Incidence in Massachusetts 1982-1990* [MDPH 1993]. This report contained cancer incidence data for a number of cancer types in cities and towns in Massachusetts. Data in the report indicated that for the time period 1982 to 1990, the town of Shelburne experienced an excess in female breast cancer cases that was statistically significant when compared to statewide rates. Further investigation by the MDPH attributed the significant elevation to the mis-assignment of breast cancer cases among residents of Buckland and Charlemont to Shelburne. Subsequently, the MCR released two additional years of data, which included the years 1991 and 1992. This report reviewed cancer incidence data for two time periods: 1982 to 1986 and 1987 to 1992. This publication reported an increased incidence of breast cancer among women in Shelburne during the later time period, 1987 to 1992 [MDPH 1995]. However, the increase was no longer statistically significant.

In February 1997, the MDPH, Bureau of Environmental Health Assessment (BEHA) published a health consultation entitled, *Cancer Incidence and Down Syndrome Prevalence in the Deerfield River Valley, Massachusetts* [MDPH 1997]. This report recommended that due to the increase in the incidence of breast cancer over time, an in-depth analysis of breast cancer incidence should be conducted for the town of Shelburne.

Therefore, the Community Assessment Unit (CAU) of the MDPH, BEHA further investigated breast cancer incidence in the town of Shelburne. During the time period evaluated (1982 to 1994), no cases of breast cancer were observed among males in Shelburne. As a result, this investigation focused specifically on the incidence of breast cancer among women in the town of Shelburne. Breast cancer incidence in Shelburne has been descriptively evaluated and available data on factors that may play a role in the development of breast cancer have been examined.

II. OBJECTIVES

This evaluation is a preliminary investigation that analyzes descriptive health outcome data for breast cancer. This review provides a comparison of the incidence of breast cancer in Shelburne with the incidence of breast cancer in the state. Using the state as a comparison population provides stability and replicability of incidence rates. The primary focus of this investigation was to evaluate the temporal and geographic pattern of breast cancer in Shelburne and the possible role that risk factors may play in breast cancer incidence in the town.

Information from descriptive analyses such as this evaluation cannot determine the causal relationship between the development of the cancer and associated risk factors. However, this type of analyses may suggest that a common etiology (or cause) is possible and can serve to identify areas where further public health investigations or actions may be warranted. Descriptive analyses may also indicate that an excess of well established risk factors that have been associated with a disease exist in a certain geographic area. The purpose of this investigation is to report our findings and discuss them in the context of available information to determine whether recommendations for follow-up are warranted.

The specific objectives of this investigation were:

to evaluate breast cancer incidence in Shelburne during the time period 1982 to 1994;

to evaluate the geographic distribution of breast cancer cases in Shelburne in order to determine whether a geographic pattern of cases exists in certain areas of the town which suggests that environmental factors may have played a role;

to review available descriptive information reported to the MCR related to risk factors for developing breast cancer;

to discuss the results of this evaluation in the context of the available scientific literature on breast cancer to determine whether further investigation or public health action is warranted.

III. METHODS

A. Case Identification

Breast cancer incidence data for the years 1982 to 1994 were obtained for the town of Shelburne from the MCR of the MDPH, Bureau of Health Statistics, Research, and Evaluation. The observed number of breast cancer cases were derived from cases reported to the MCR as primary site breast cancer cases diagnosed in Shelburne residents between the years 1982 to 1994. Cases were selected for inclusion based on the address of residence reported to the hospital or reporting facility at the time of diagnosis.

The MCR began collecting information on individuals diagnosed with cancer in the state of Massachusetts in 1982. All newly diagnosed cancer cases are required by law to be reported to the MCR within six months of the date of diagnosis [M.G.L.c.111B]. The 12-year period 1982 to 1994 constitutes the period for which the most recent and complete data were available at the time of this analysis.

The observed number of breast cancer cases reported for Shelburne are in some instances slightly different from the observed number of cases in the MCR report, *Cancer Incidence in Massachusetts 1987-1994 City and Town Supplement* [MDPH 1997b]. This is because the data contained in the MCR *City and Town Supplement* reflect information reported to the MCR as of March 20, 1997. The MCR data are continually quality controlled so that corrections may be made in subsequent reports. For this analysis, each breast cancer case was individually reviewed resulting in further refinement of the data included in the *City and Town Supplement*.

The MCR data file occasionally contains duplicate reports of single cases. This analysis accounts for these cases by removing the duplicate cases of breast cancer while including multiple primary breast cancer cases. Duplicate cases are additional reports of the same primary site cancer case. A multiple primary cancer case is defined by the MCR as a new cancer of the same histology (or cell type) as an earlier cancer, if diagnosed in the same primary site (original location in the body) more than two months after the original diagnosis [MCR 1996]. The decision that a case was a duplicate and should be excluded from the analyses was made by the MCR after consulting with the reporting facilities and obtaining additional information regarding the histology and pathology of the case.

B. Calculation of Standardized Incidence Ratios (SIRs)

To determine whether an elevated number of breast cancer cases occurred in the town of Shelburne for the time period evaluated, breast cancer incidence data were analyzed by age and sex to compare the observed number of breast cancer cases in Shelburne to the number of

cases that would be expected based on the statewide breast cancer incidence. Standardized Incidence Ratios (SIRs) were calculated for three time periods: 1982 to 1986, 1987 to 1994, and the entire 12-year period 1982 to 1994.

An SIR is an estimate of the occurrence of cancer in a population relative to what might be expected if the population had the same cancer experience as some larger comparison population designated as "normal" or average. Usually the state as a whole is selected to be the comparison population. Using the state of Massachusetts as a comparison population provides a stable population base for the calculation of incidence rates. As a result of the instability of incidence rates based on small numbers of cases, SIRs were not calculated when fewer than five cases were observed.

Specifically, an SIR is the ratio of the observed number of cancer cases to the expected number of cases, multiplied by 100. An SIR of 100 indicates that the number of cancer cases observed in the population being evaluated is equal to the number of cancer cases expected in the normal population. An SIR greater than 100 indicates that more cancer cases occurred than expected; an SIR less than 100 indicates that fewer cancer cases occurred than expected. Accordingly, an SIR of 150 is interpreted as 50% more cases than the expected number; an SIR of 90 indicates 10% fewer cases than expected.

Caution should be exercised, however, when interpreting an SIR. The interpretation of an SIR depends on both the size and the stability of the SIR. Two SIRs can have the same size but not the same stability. For example, an SIR of 150 based on four expected cases and six observed cases indicates 50% excess in cancer, but the excess is actually only two cases. Conversely, an SIR of 150 based on four hundred expected cases and six hundred observed cases represents the same 50% excess in cancer, but because the SIR is based upon a greater number of cases, the estimate is more stable. It is very unlikely that 200 excess cases of cancer would occur by chance alone.

Further, in order to calculate incidence rates, it is necessary to obtain accurate population information. The population figures used in this analysis were interpolated based on 1980 and 1990 census data for the town (U.S. Department of Commerce 1980, 1990). Midpoint population estimates were calculated for each time period evaluated. To estimate the population between census years, an assumption was made that the change in population occurred at a constant rate throughout the ten-year interval between each census.

C. Calculation of the 95% Confidence Interval

In addition to calculating SIRs, the statistical significance of each SIR was also assessed. A 95% confidence interval (95% CI) was calculated for each SIR to determine if the observed number of cases is significantly different from the expected number or if the difference may be due solely to chance (Rothman and Boice 1982). A 95% confidence interval is a method of assessing the magnitude and stability of an SIR. Specifically, a 95% CI is the range of estimated SIR values that have a 95% probability of including the true SIR for the population. If the 95% CI range does not include the value 100, then the study population is significantly different from the comparison or "normal" population. "Significantly different" means there is less than 5% chance that the observed difference is merely the result of random fluctuation in the number of observed cancer cases.

For example, if a confidence interval does not include 100 and the interval is above 100 (e.g., 105-130), then there is statistically significant excess in the number of cancer cases. Similarly, if the confidence interval does not include 100 and the interval is below 100 (e.g., 45-96), then the number of cancer cases is statistically significantly lower than expected. If the confidence interval range includes 100, then the true SIR may be 100, and it cannot be concluded with sufficient

confidence that the observed number of cases is not the result of chance and reflects a real cancer increase or decrease. Statistical significance was not assessed when fewer than five cases were observed.

In addition to the range of the estimates contained in the confidence interval, the width of the confidence interval also reflects the stability of the SIR estimate. For example, a narrow confidence interval (e.g., 103-115) allows a fair level of certainty that the calculated SIR is close to the true SIR for the population. A wide interval (e.g., 85-450) leaves considerable doubt about the true SIR, which could be much lower than or much higher than the calculated SIR. This would indicate an unstable statistic.

D. Stage at Diagnosis

Staging categorizes the extent of disease and its spread at the time of diagnosis. Breast cancer survival correlates strongly with early stage diagnosis of cancer, especially with cancer limited to the breast (local or Stage I). Screening improves the odds of breast cancer diagnosis at an early stage. Hence, an evaluation of staging information can help to determine whether cancer patients in a given area are being diagnosed at an early or late stage of disease. Such information may serve to indicate whether individuals residing in Shelburne are receiving adequate breast cancer screening. This information can then be used to identify cancer patterns within communities where further public health intervention may be warranted. An increased use of screening results in early detection of the cancer, and therefore may indicate an increase in the town-wide incidence of this cancer. Staging information reported to the MCR at the time of diagnosis for breast cancer cases in Shelburne and the state of Massachusetts were analyzed and compared.

This analysis defines stage in four categories: localized, regional, distant, or unknown. Localized breast cancer represents a diagnosis that the tumor is invasive but the cancer is confined to the breast. Regional indicates that the tumor has spread beyond the organ of origin (breast). This may include spread to adjacent tissues or organs, lymph nodes, or both [MCR 1996]. Distant indicates that the cancer has metastasized or spread to organs other than those adjacent to the organ of origin, or to distant lymph nodes or both [MCR 1996]. Some of the cases reported to the MCR are reported with an unknown stage. This indicates that at the time of reporting the tumor had not been staged.

This report only assesses breast cancer reported as localized, regional, distant, or unknown. In 1992, the MCR began collecting data regarding breast cancer cases categorized as in-situ breast cancer. Breast cancer in-situ is defined as malignant cells within the breast ductal-lobular system without evidence of invasion of neighboring tissues [Harris, et. al. 1996]. As a stage of cancer, in-situ represents the earliest detectable stage of the disease and therefore has a more favorable prognosis. In-situ cases of breast cancer have not been included in this report because these data have only been available since 1992.

E. Socioeconomic Status Data

Indicators of socioeconomic status such as income and education level are factors that correlate with risk factors for an increased risk of breast cancer such as having few or no children and age at first childbirth [Henderson, et. al. 1996]. Socioeconomic factors may also be related to cultural beliefs and attitudes that may account for the difference of race on breast cancer stage [Lannin DR, et. al. 1998]. For example, breast cancer is more frequently diagnosed at an advanced stage among African American females than in white females. Data from the U.S. Census Bureau for three variables were evaluated as indicators of socioeconomic status for Shelburne to determine whether these factors may be related to increased rates of breast cancer in this area. The three variables evaluated are: percentage of individuals with a Bachelor degree or higher, median

household income, and percentage of individuals below the poverty level [U.S. Census Bureau 1990].

F. Reproductive Factors

Reproductive factors such as late age at first full-term pregnancy, low parity (i.e., few or no children), early age at menarche and late age at menopause, are well established risk factors related to the development of breast cancer. Information regarding all of these risk factors is not readily available. However, the MDPH, Bureau of Health Statistics, Research and Evaluation collects information for all births that occur in the state of Massachusetts. Information for the mean age at first birth and the percentage of women having a first, second, and third birth was reviewed for Shelburne women ages 15 to 44. These data were evaluated for the 15-year time period 1975 to 1990 in order to determine whether a change in these factors over time in Shelburne may be related to increased rates of breast cancer. The prevalence of these risk factors in both Shelburne and the state of Massachusetts will be discussed.

G. Determination of Geographic Distribution

The geographic distribution of breast cancer cases in Shelburne was determined using available information from the MCR regarding the address of residence at time of diagnosis for each breast cancer case. This information was mapped for each individual using the computer mapping software MapInfo (MapInfo 1996). The computer mapping allowed for locating the exact residence of each case. In instances where the address information was incomplete (i.e., did not include specific streets or street numbers), efforts were made to research those cases using telephone books and residential lists issued within two years of an individual's diagnosis.

IV. RESULTS

A. Cancer Incidence Analysis

1. Previous Data 1982 to 1990

Data reported from the MCR for the time period 1982 to 1990 highlighted Shelburne as one of several towns which had a statistically significant elevation of breast cancer in females (SIR=202; 95% CI=137-287)[MDPH 1993]. As shown in Table One, 31 cases of female breast cancer were observed in Shelburne during this time period when approximately 15 were expected.

Further investigation determined that this elevation was due to the mis-assignment of Buckland and Charlemont residents to the Shelburne and Shelburne Falls areas. To provide a point of reference, Shelburne's boundaries have been delineated in Figure 1 and Figure 2. Specifically, eleven cases reported as Shelburne residents did not reside in Shelburne. Of the eleven cases reported as Shelburne residents, eight actually resided in Buckland and three in Charlemont. Once the eleven cases were correctly assigned, the SIR for breast cancer was re-calculated. Results from the new calculations indicated that although the incidence of breast cancer remained elevated it was no longer a statistically significant result. Twenty cases of breast cancer were observed in Shelburne while approximately 15 were expected (SIR=133; 95% CI=81-206).

2. Previous Data 1982 to 1992

The MCR subsequently released cancer incidence data for the years 1982 to 1992, which included two additional years of data. This report did not highlight Shelburne as having a statistically significant elevation of breast cancer [MDPH 1995]. However, as shown in Table 1, female breast cancer incidence in Shelburne remained elevated during this time period (28

observed versus 19.3 expected; SIR=145; 95% CI=96-210) [BEHA 1997]. Data for earlier part of this time period (1982 to 1986) indicated that breast cancer incidence in Shelburne was approximately equal to expected based on statewide breast cancer rates [BEHA 1997]. There were 10 cases of female breast cancer observed and approximately 8 cases were expected (SIR=123).

Breast cancer incidence during the later time period, 1987 to 1992, accounted for most of increase observed during the entire 1982 to 1992 time period. Between the years 1987 to 1992, 18 cases of breast cancer were observed in Shelburne and approximately 11 cases were expected (SIR=161; 95% CI=95-254). Among females in Shelburne, 7 more cases of breast cancer than expected were diagnosed during this period. This elevation was not statistically significant (refer to Table 1) [BEHA 1997].

3. Recent Data 1993 to 1994

Two additional years of data have become available for analyses in the most recent report published by the MCR, *Cancer Incidence in Massachusetts 1987-1994*, [MDPH 1997]. Shelburne is highlighted in this report as having a statistically significant elevation of female breast cancer (27 cases observed versus 14.8 expected, SIR=183, 95% CI= 121-266). This data is also presented in Table 1.

During the present investigation, additional research and mapping of the most recent MCR data file (1987 to 1994) again revealed the mis-assignment of two more cases of breast cancer to the town of Shelburne. One case was re-assigned to Charlemont and one case was re-assigned to Buckland. Once the two cases were correctly assigned breast cancer SIRs among females in Shelburne were re-calculated for time periods 1982 to 1994, 1987 to 1994, and 1982 to 1986. The results are presented in Table 2.

During the period 1982 to 1994, female breast cancer incidence was statistically significantly elevated in Shelburne. A total of 35 cases were diagnosed among Shelburne women where approximately 23 were expected during this time period, resulting in an excess of 12 cases. This 50% increase above the statewide rate of breast cancer in the town of Shelburne (SIR=150) was statistically significant (95% CI=105-209). During the earlier time period (1982 to 1986) females in Shelburne experienced an excess of two breast cancer cases over the expected number of cases. Among females, 10 cases were observed where approximately 8 would have been expected based on the statewide incidence (SIR=124, 95% CI=59-228).

During the later time period, 1987 to 1994, a total of 25 cases were diagnosed among Shelburne females where approximately 15 cases would have been expected based on the statewide rate (SIR=167). This represents a 67% increase above the statewide rate of breast cancer in the town of Shelburne. In total, 7 additional cases of breast cancer were diagnosed in Shelburne during the years 1993 and 1994. These results are summarized in Table 2.

4. Geographic Distribution

Place of residence at the time of diagnosis was mapped for each breast cancer case to assess any possible geographic concentration of cases. A qualitative evaluation was conducted to determine whether any cases appeared to be concentrated in area(s) within the town. The cases did not appear to be distributed in any specific pattern in the town. In some areas where cases appeared to be more geographically concentrated than others, further examination showed that the apparent concentrations were located in areas of dense population. In Shelburne, the majority of cases resided in the downtown area, where the population density is greater than other areas of town.

B. Evaluation of Risk Factors for Breast Cancer

1. Age Distribution

Age specific data on the observed number of breast cancer cases in Shelburne indicate that the elevations observed among women in Shelburne were, for the most part, among women in the older age groups. The majority of individuals diagnosed with breast cancer during 1982 to 1994 in Shelburne were over age 50 (69%). The pattern of incidence during the 12-year period indicates that, with the exception of a peak in the 40 to 44 year age group, breast cancer incidence rose steadily with increasing age, peaking in women over the age of 85. Peaks in breast cancer incidence were observed primarily in the older ages groups: 50 to 54, 65 to 69 and 70 to 74. Due to the small number of cases occurring in each age group, information regarding the exact number of cases in each age group is not disclosed in order to preserve the confidentiality of the cases. This data is presented in Figure 3.

Although SIRs calculated for the town of Shelburne are adjusted according to age, calculation of age group specific SIRs show that an increase in cases among the younger age groups is largely responsible for the overall observed increase in Shelburne. Specifically, the age group specific SIRs for Shelburne show a peak in incidence among females aged 40 to 44 years. The breast cancer cases in this peak account for approximately 26% (n=9) of the total distribution during the years 1982 to 1994. Review of the age-distribution by time period indicates that the peak in younger cases primarily occurred during the second time period (1987 to 1994). Of the nine cases with an age range of 40 to 44 years at the time of diagnosis, two were diagnosed during the first time period (1982 to 1986) and seven were diagnosed during the second time period (1987 to 1994). The annual distribution of these nine cases appeared at random and dispersed throughout the time period.

The peak observed in individuals over the age of 85, represents 20% (n=7) of the total female breast cancer cases diagnosed during period 1982 to 1994. All of these cases were diagnosed during the second time period, 1987 to 1994. These data are presented in Figure 4.

2. Evaluation of Stage at Diagnosis

The distribution of stage at diagnosis for breast cancer cases in Shelburne and Massachusetts is presented in Figures 5 through 7. In Shelburne, during the time period 1982 to 1994, the distribution of stage at time of diagnosis shows a shift towards earlier stage cases with the majority (69%) of cases diagnosed as local stage. The percentage of regional stage breast cancer was 23%. Only 3% of the cases were diagnosed at distant stage, and only a small percentage (6%) were of an unknown stage.

A similar distribution of stage at diagnosis was observed among breast cancer cases in the state of Massachusetts during this time period, with Massachusetts having approximately the same percentage of cases with unknown stage (6%). Comparison of stage at diagnosis for breast cancer cases in Shelburne and Massachusetts showed a slightly greater percentage of earlier (local) stage cases in Shelburne than in the state (69% versus 59%). These data reveal that during 1982 to 1994 in both the state as a whole and the town of Shelburne, the majority of the breast cancer cases were diagnosed at an early stage (localized) as opposed to a later stage of the disease (regional or distant). These data are presented in Figure 5.

When staging information for Shelburne and the state as a whole were evaluated by separate time periods (1982 to 1986 and 1987 to 1994) the data revealed a shift toward an increasing percentage of localized stage cancers during 1987 to 1994 (refer to Figure 6). Both Shelburne and the state as a whole showed an increase in the proportion of breast cancer cases diagnosed at an early stage (localized) during the second time period in comparison to the first time period

evaluated in this report. In addition, Shelburne showed a larger increase in the proportion of local diagnostics during the 1987 to 1994 time period than Massachusetts. In Shelburne, during 1982 to 1986 only half (50%) of all female breast cancer cases were diagnosed at local stage (see Figure 7). The percentage diagnosed at regional stage was 30%. This pattern is similar to that of the state. However, during the later years 1987 to 1994, 76% of all female breast cancer cases in Shelburne were diagnosed as localized. In the state of Massachusetts during this same time period, approximately 62% were diagnosed as localized.

Staging information evaluated for the two age groups largely responsible for the overall observed increase in breast cancer incidence in Shelburne (40 to 44 and over age 85) indicate that the majority of individuals in these age groups were diagnosed at an early stage (localized) of the disease. Of the nine female's aged 40 to 44 at the time of diagnosis, eight had localized staging and one had regional staging. Of the seven women over the age of 85, four had localized staging, two had regional staging, and one had an unknown stage.

The increase in breast cancer screening during the mid 1980s most likely resulted in an increased percentage of cases detected at an earlier stage of the disease (localized) and a decrease in the percentage of cases diagnosed at a more advanced stage of the disease (distant). Data on stage at diagnosis show that more than half of the breast cancer cases diagnosed in Shelburne were detected early. Breast cancer screening has increased at varying rates across Massachusetts communities. Therefore, it is possible that many women diagnosed with breast cancer in the town received screening for early detection of breast cancer.

3. Socioeconomic Status

Increased socioeconomic status has been correlated with factors associated with an increased risk of developing breast cancer. The socioeconomic status of individuals residing in the town of Shelburne was evaluated and compared to the state as a whole. Indicators of socioeconomic status in Shelburne and Massachusetts are presented in Table 3. Compared to the state of Massachusetts, Shelburne has a lower percentage of individuals with a college education (24%), a lower median household income (\$27,639), and a greater percentage of individuals below poverty level (10%). In Massachusetts, the percentage of individuals with a college education is 27%, the median household income is \$36,952 and the percentage of individuals living below poverty level is 9%. These data show that the town of Shelburne displays lower socioeconomic characteristics than the state as a whole. However, it is important to recognize that the data regarding indicators of socioeconomic status presented here, represent data for the whole town and are not necessarily representative of the individual cases.

4. Reproductive Factors

Epidemiologic studies have shown that reproductive factors such as late age at first full-term pregnancy, early age at menarche, low parity (i.e., having few or no children) and late age at menopause increases a women's risk for developing breast cancer. Available data regarding mean age at first childbirth and parity among Shelburne women were reviewed to determine whether these factors might have changed over time in the town.

Age at First Birth:

Information regarding mean age at first birth among women ages 15 to 44 was evaluated for a 15-year period during 1975 through 1990. During this period the mean age at first birth increased by 3 years among Shelburne women. The mean age at first birth was 26 in 1975 and 29 in 1990. The mean age at first childbirth in Shelburne women was also slightly greater than that observed among women in the state as a whole for the entire 15-year time period. In Massachusetts, the

mean age at first childbirth was 23 in 1975 and 26 in 1990. These data are summarized in Figure 8.

Epidemiologic studies have shown that late age (i.e., over the age of 30) at first full-term pregnancy can increase a women's risk for developing breast cancer. In Shelburne during the 15-year time period 1975 through 1990, the percentage of women having a first child over age 30 increased, and the percentage of women having a first child under the age of 30 decreased. In 1975, all (100%) women in Shelburne who gave birth to a first child were under the age of 30. However, by 1990 only 75% of first childbirths in the town were among women under the age of 30. This represents a decrease in the percentage of first births among women at younger ages. In addition, 25% of first childbirth's in the town were among women over the age of 30, representing an increase in the percentage of first births among older women. These data are summarized in Table 9.

Similarly, the percentage of women having a first child over age 30 in the state of Massachusetts increased and the percentage of women having a first child under age 30 decreased steadily. Between the years 1975 to 1990 the percentage of first births among women under the age of 30 declined from 92% to 71%. The percentage of women over the age of 30 who had a first child increased in the state from 8% in 1975 to 29% in 1990. This information indicates that women under the age of 30 in the state continue to have fewer children than their older counterparts. These data are summarized in Table 10.

Parity:

Parity was evaluated by reviewing the percent of total births in Shelburne that were a first birth, second birth, or third or more birth during the 15-year period 1975 to 1990. In Shelburne, the total number of live births remained the same from 1975 to 1990. However, the degree of parity among Shelburne women decreased over this 15-year period.

The percentage of first births among women in Shelburne decreased from 41% in 1975 to 27% in 1990. The percentage of Shelburne women having a second birth remained fairly constant throughout the time period evaluated. In 1975, 41% of the total births in Shelburne were second births, and in 1990, 43% of the total births were second births. In Shelburne women, the percentage of third births increased from 17% in 1975 to 30% in 1990. These data suggest that the reduction in parity observed in Shelburne may be related to a decline in women having first and second births.

In contrast, in the state of Massachusetts as a whole, the percentage women having a first birth increased from 42% in 1975 to 52% in 1990. Similarly, in contrast to Shelburne, the percentage of second births among Massachusetts's women decreased from 32.3% to 19.2%. Among women in the state as a whole, the percent of third births increased from 24.9% in 1975 to 28.2% in 1990. In contrast to the trends observed in Shelburne, in Massachusetts, the decrease in the number of births among women appears to be associated with a decrease in second and third births.

V. DISCUSSION

During the time period 1982 through 1994 the incidence of female breast cancer was statistically significantly elevated in Shelburne. This elevation is primarily due to an increase in incidence during 1987 to 1994. For both time periods the age-specific incidence rates indicated two peaks in incidence occurring among women age 40 to 44 years in women over the age of 85.

Evaluation of the geographic distribution of breast cancer cases displayed no discernible pattern of clustering in the town. The majority of cases resided in the downtown area, where the population density is greater than other areas of town. In addition, no pattern was observed

between the geographic distribution of breast cancer cases and the location and type of hazardous waste sites in Shelburne. However, it should be noted that this evaluation only qualitatively describes the geographic pattern of breast cancer cases in relationship to hazardous waste sites in Shelburne.

In the United States from 1973 to 1987 there was a 20% increase in breast cancer incidence, but only a 2% increase in mortality from breast cancer (Henderson et. al, 1996). While age adjusted mortality rates for breast cancer have remained constant since 1930; breast cancer incidence rates have been rising over the past several decades (Kelsey and Gammon 1990). The incidence of female breast cancer in Massachusetts has been increasing since 1982 with some leveling off occurring in the late 1980's (MDPH, 1997a). In Massachusetts, the incidence of female breast cancer has increased from 100 cases per 100,000 people during 1982 to 1986, to 117.2 per 100,000 people during 1987-1992 (MDPH 1997a). A portion of this increase in incidence is likely attributed to early detection brought on by mammography utilization.

However, improved detection is not likely to be the only factor associated with the increase in incidence rates. The established risk factors account for less than half of the reported breast cancer cases in the United States. Thus, there is speculation concerning the role that other potential risk factors such as diet, physical activity, occupation, and the environment may contribute to breast cancer (Falck 1992).

According to the American Cancer Society (ACS), breast cancer is the second major cause of cancer deaths in women, surpassed only by lung cancer deaths (ACS 1998). The ACS estimates 178,700 new cases of breast cancer were diagnosed among women in the United States during 1998 (ACS 1998). The ACS also estimates that in 1998, 43,900 individuals died of breast cancer (43,500 deaths in females, and 400 deaths among males).

Breast cancer has the highest incidence rate of all cancers among women aged 35 and above, with higher incidence rates in older age groups (Devesa et. al, 1995). Breast cancer incidence and age are related; incidence steadily increases from age 35-50, and sharply increases in post-menopausal women over the age of 50 (Kessler, 1992). The majority of cases occur in women above 50 years. In Shelburne, a similar pattern of incidence was observed where the majority of breast cancer cases were diagnosed over age 50 and incidence increased with increasing age. However, a peak in incidence was also observed in Shelburne women aged 40-44 years.

Five-year survival rates for breast cancer are 82% among white women and 66% among black women (Briton and Devesa, 1996). In that study, over 50% of breast cancer in white women were diagnosed as localized and 40% of breast cancer in black women was localized. Survival is 86% for women with a localized diagnosis but 20% for a distant diagnosis.

Screening women for breast cancer by mammography detects cancer at an early, asymptomatic stage. As a result, early diagnosis of breast cancer by mammography may yield an increased incidence of the disease because it was previously not detected in this group of people. The National Cancer Institute (NCI) recently reviewed screening data and determined mammography reduces deaths for women in their 40s by 17 percent. The NCI recommends women in their 40s be screened every one to two years if they are at average risk for breast cancer, those at high risk should seek further medical advice (NCI 1997). Mammography has resulted in an increase in detection of breast carcinoma in situ (Morrow et al, 1996). The incidence of localized breast cancer in women 50 and older increased 50% from 1979 to 1986, but ductal carcinoma in situ increased 235%. Almost all carcinoma in situ are found using mammography, because they are too small to be detected otherwise.

Evaluation of the stage at diagnosis provides an indication of the utilization of breast cancer screening in Shelburne. When stage at diagnosis was evaluated in Shelburne, Shelburne

generally had a greater percentage of early stage cancers in both of the time periods evaluated. In addition, the town of Shelburne generally experienced a greater percentage of these cancers annually than the state of Massachusetts. This may indicate that screening and early detection practices are being used more often resulting in a greater number of cases detected in this area.

There are several known risk factors for breast cancer and many potential risk factors that are under current investigation (Henderson et. al, 1996). The majority of known risk factors for breast cancer are attributed to genetics and hormones. A family history of breast cancer, early onset of menstruation, late age at menopause, never having had children, and late age at first full term pregnancy have been identified as risk factors for breast cancer in females. In addition, higher education and socioeconomic status are factors thought to be related to risk factors for higher rates of breast cancer. Potential risk factors also include occupational or environmental exposure to chemicals, diet and weight gain, alcohol, benign breast disease and factors in the intrauterine environment before birth. Reduction of the risk of breast cancer may be possible by reducing a woman's lifetime exposure to estrogen. Estrogen exposure can be reduced by exercise, a full term pregnancy before age 20, and lactation.

Higher breast cancer screening participation rates are typical among females of high socioeconomic status (Segnan, 1997). However, socioeconomic data evaluated for Shelburne indicate that Shelburne has a lower socioeconomic status when compared to Massachusetts as a whole. It is important to note that the difference in socioeconomic status between Shelburne and the state is not substantial and therefore this data should be interpreted with caution. Further, socioeconomic data for Shelburne was not specific to the individual cases themselves.

Data related to reproductive factors among Shelburne women indicated that the mean age at first full term pregnancy increased by 3 years from 26 in 1975 to 29 in 1990. The mean age of Shelburne women at first full term pregnancy was over two to three years greater than that of women in the state of Massachusetts. In both Shelburne and Massachusetts, the mean age at first childbirth increased from 1975 to 1990. In addition, parity decreased from 41% in 1975 to 27% in 1990. This data suggests that factors related to an increased risk of developing breast cancer might be related to the current increase in incidence observed statewide and nationally.

There is a strong relationship between the hormone estrogen and breast cancer (Henderson et. al. 1996). Research has found that breast cancer patients have higher blood estrogen levels when compared to women without breast cancer. Cumulative exposure of the breast to estrogen and/or progesterone affects the rate of breast cell division. Several factors affect lifetime estrogen exposure. Menarche and regular ovulatory cycles at an early age result in increased exposure to estrogen and increased risk of breast cancer. Physical activity in young girls can delay menarche, and therefore reduce lifetime exposure to estrogens (Henderson et. al. 1996). Age at menopause is another factor; women who experience menopause before age 45 have half the risk of breast cancer than do women who experience menopause after age 55. Women who have their first child before age 30 have a decreased risk of breast cancer (Brinton et. al. 1983); the risk of breast cancer also decreases with subsequent births. Lactation is protective against breast cancer because it results in delayed ovulation, which reduces estrogen levels. Women who have their first child at an older age and women who do not have children are at an increased risk for breast cancer, but the causal biologic mechanisms are unknown.

The hormone estrogen is a suspected risk factor for the development of breast cancer. Studies of oral contraceptive use and breast cancer have mixed results and are inconclusive (Henderson & Bernstein 1996). Long-term use of estrogen replacement therapy has shown an increase in breast cancer risk (40% after 15 years of use), but no increase has been observed with short-term use. Research of women using estrogen and progestin has also found similar increased risks of breast cancer with five to nine year's use. This risk was increased to 71% in women 60-64 years (Colditz et. al. 1995).

Factors in the intrauterine environment may also be risk factors for breast cancer (Ekbom et. al. 1997). A reduced risk of breast cancer was found in women whose mothers had pregnancy toxemia, and an increased risk was found in women who had neonatal jaundice, were born before 33 weeks gestation, or were dizygotic twins. These factors may be related to estrogen exposure. Toxemia is associated with a low level of estrogen; jaundice, prematurity, and twins are associated with high levels of estrogens.

Lifestyle factors such as diet, and physical activity are also related to breast cancer risk. Diet modifies menarche and weight, but studies of body fat and breast cancer are contradictory and more research is needed (Henderson et. al. 1996). Body weight is also a risk factor, for women age 60 and older a 10-kilogram weight increase results in an 80% increase in breast cancer risk. Some studies have shown that drinking alcohol is a risk factor. A recent study by Swanson et. al. (1997) found a 1.7 times increased risk of breast cancer among women who drank 14 or more drinks per week.

Physical activity is another lifestyle factor related to breast cancer. Exercise may reduce cumulative exposure to cyclic estrogens and influence an energy balance that inhibits mammary carcinogenesis (Thune et. al. 1997). Recent research has shown a 37% reduction in risk of breast cancer among women who exercise regularly compared to sedentary women. Issues of diet and exercise and their relationship to breast cancer need more research. Diet and exercise are modifiable lifestyle factors, and changes in these factors may reduce the risk of breast cancer.

Genetically inherited breast cancer accounts for 5% to 10% of all breast cancers (Harris et. al, 1996). Recent scientific research has identified genes related to breast cancer. These genes are BRCA1, BRCA2, and p53, which can be inherited in forms capable of conferring increased breast cancer susceptibility. These breast cancer genes are believed to act as tumor suppressors (i.e., their function is to suppress the formation of tumors). Individuals are born with two copies of every gene. If an individual inherits a mutation, which alters its tumor suppressor capacity, only one copy of the tumor-suppressor gene is acting to suppress tumor formation. If this copy of the tumor suppressor gene is then inactivated by a non-inherited event (such as estrogen exposure), the chance of developing cancer increases. Thus, women who inherit mutated versions of this gene are at higher risk of developing breast cancer than women who do not carry mutated versions of the gene (Harris et. al., 1996). Early age of cancer onset, bilateral breast cancer, and appearance of other cancers such as ovarian, colon, prostate or endometrial cancer (Garber & Weber, 1996) often distinguish genetically inherited breast cancer.

The BRCA1 gene has been researched intently. Women who have this mutation pass it on to approximately half of their children (Weber & Garber, 1996). Females who inherit the BRCA1 mutations and have a family history of breast cancer have an 85% risk in their lifetime of developing breast cancer. However, normal functioning of the BRCA1 gene protects against developing breast cancer. It is estimated that 1 in 600 U.S. women have genetic BRCA1 mutations. As mutations on BRCA1 are isolated and more breast cancer genes are identified, the true rate of cancers related to genetics or family history can be determined.

Specific ethnic groups have been found to have a high incidence of certain BRCA1 mutations, and thus a high incidence of breast cancer. For example, 1% of the Ashkenazi Jewish population is estimated to have a BRCA1 mutation (Struewing et. al. 1995). In a recent study by Fitzgerald et. al., (1996) 21% of Jewish women with breast cancer under age 40 were found to be carriers of this mutation. These prevalence estimates may be elevated because they are based on people chosen for research because they had a high frequency of the gene phenotype in their families (Bryant 1996). Other BRCA1 and BRCA2 mutations have been found in several different ethnic groups (i.e., Norwegians, Icelanders, Japanese, Swedes) (Keoun, 1997).

Many epidemiological studies have estimated the effect that having relatives with breast cancer influences the increased likelihood of developing the disease. When a first-degree relative has

breast cancer (i.e., mother or sister), there is a two to three times increased risk of breast cancer compared to women whose relatives do not have breast cancer (Henderson et al. 1996). When multiple first-degree relatives have breast cancer, there is a five times increased risk of breast cancer. When a first degree relative has bilateral premenopausal breast cancer, the risk increases to nine times.

Several genetic clinical syndromes have been identified that involve breast cancer (Weber & Garber, 1996). Breast-ovarian cancer syndrome results from the BRCA1 mutation as mutation carriers also have an excess risk of ovarian cancer. Li-Fraumeni syndrome has an autosomal dominant inheritance and is characterized by soft-tissue sarcomas and an excess of breast cancer. Cowden syndrome, Muir syndrome, and ataxia-telangiectasia are also associated with increased incidence of breast cancer.

Women with benign breast disease (i.e., chronic cystic or fibrocystic disease or fibroadenoma) may be at increased risk for breast cancer (Henderson et. al., 1996). Some women diagnosed with benign breast disease may have atypical changes in the breast epithelium, and epithelial lesions may be a precursor of breast cancer. Future research on the types of benign breast disease can identify subgroups at risk for breast cancer.

Goldberg and Labreche (1996) reviewed the literature on occupational risk factors related to breast cancer. From this review, associations were found between breast cancer and employment as a cosmetologist, beautician, and in the pharmaceutical industry; and potential associations with chemists and occupations exposed to low frequency electromagnetic fields. No association with breast cancer was found with workers in dry cleaning, textiles, or nuclear industry. Occupational risk factors for breast cancer need further investigation through population-based studies of women in specific industries.

While definitive information about the role of environmental factors in breast cancer is not available, studies are currently underway to evaluate potential links between breast cancer and environmental factors such as pesticides and electromagnetic fields (Kelsey and Gammon 1990, Falck 1992). The primary environmental risk factor that has been identified in relation to breast cancer is exposure to ionizing radiation, as evidenced by follow-up studies of atomic bomb survivors.

Substances in the environment; for example, pesticides and PCBs, have been hypothesized to be related to breast cancer. Chlorinated hydrocarbon pesticides (i.e., DDT and DDE) were commonly used in the 1950s and 1960s (Millikan et al., 1995). These compounds concentrate in the food chain and accumulate in human tissue. Xenoestrogens are compounds that affect estrogen production and metabolism, and may induce breast cancer (Davis et. al, 1993). Some chemicals present in the environment such as DDT, herbicides, and polycyclic aromatic hydrocarbons acts as xenoestrogens and stimulate estrogen and some promote breast cancer experimentally. Xenoestrogens can cause genetic mutations in breast cancer susceptibility genes, and the genetic-environmental interactions of these compounds needs to be further studied in large populations. Exposure to xenoestrogens is a potentially modifiable risk factor and avoidance of these compounds may be a method of primary prevention of breast cancer.

A study, conducted at the Mt. Sinai School of Medicine in New York, explored a possible relationship between breast cancer and exposure to certain pesticides. This study, however, was of a preliminary nature, and not conclusive in its results (Wolff 1993). A recent study conducted by researchers at Harvard Medical School measured levels of DDE and PCBs in a group of women subsequently diagnosed with breast cancer (Hunter et. al. 1997). Blood serum levels of these chemicals in the women with breast cancer were compared levels in a group of women with no breast cancer. The study revealed that the median level of DDE and PCBs was lower among breast cancer patients than the women with no breast cancer. Although this study does not support the hypothesis that exposure to DDE and PCBs increases the risk of breast cancer, the

relationship between environmental risk factors and breast cancer needs to be further investigated in studies that measure individual levels and ask detailed questions about exposures to chemicals. In addition, since only total PCBs were measured, the relationship between breast cancer and various PCB congeners (i.e., specific types of PCBs) warrants further exploration.

The BEHA is presently conducting research initiatives exploring a potential relationship between breast cancer and environmental agents, including a major study, conducted by a contractor to the MDPH, on the environment and breast cancer on Cape Cod and a pilot study conducted solely by MDPH staff in Berkshire County, Massachusetts, investigating changes in congener specific serum PCB and pesticide concentrations over time in breast cancer patients. The Berkshire study aims to provide important information on data gaps identified from the Mt. Sinai study by recruiting females within weeks of their diagnosis. The primary data gaps identified in the Mt. Sinai study included the recruitment of female breast cancer patients after diagnosis and treatment had been initiated. This raised the question of whether the association observed between diagnosis of breast cancer and body burdens of PCBs/DDE as an artifact related to physiologic change after diagnosis and treatment or whether the observed association was real. The Berkshire study also aims to provide further information on data gaps identified in the recent study conducted by Harvard by measuring the levels of different congeners (or types) of PCBs and pesticides in breast cancer patients over time.

VI. LIMITATIONS

Descriptive epidemiological investigations have certain limitations, which should be considered when interpreting these data. For this investigation, only routinely collected data were analyzed. Therefore, no specific information on personal risk factors that may have contributed to the incidence of breast cancer in Shelburne were included. For instance, familial factors such as genetics and family history or information regarding dietary factors that may influence the risk of developing breast cancer were not available for inclusion in this report. Historical data were not available; therefore an evaluation of past factors that may be attributing to the risk of disease was not possible. The MCR estimates that the data file for the years 1987 to 1994 contains 90 to 95% of all reportable cases.

Descriptive studies can not test epidemiologic hypotheses, but rather describe patterns of disease occurrence and are used to formulate hypotheses or further research questions. This investigation describes the distribution of breast cancer in the town of Shelburne in relation to temporal and geographic factors. Data on genetics, diet, length of residence in Shelburne, past residential history, income, education, and other personal factors were not available for this evaluation. Other possible limitations include non-reported breast cancer cases, incorrect street addresses or ages and miss-classification of case status.

Individual risk factors such as family history of breast cancer, age at menarche or menopause, or exposure to chemicals or other environmental factors was not available. Information such as the median household income, educational level, age at first birth and parity are indicators of risk factors for developing breast cancers. These factors were evaluated for the town in general and may not necessarily be applicable to individual risk of developing breast cancer.

VII. CONCLUSIONS

Based on the data evaluated, a statistically significant elevation in breast cancer was observed in the town of Shelburne during the years 1982 through 1994. This elevation is primarily due to an increase in incidence during the later time period, 1987 to 1994.

The age distribution of breast cancer cases revealed that the majority of cases (69%) were diagnosed in women greater than age 50. The incidence of breast cancer appeared

highest among women age 40 to 44 years and in women over the age of 85. The majority of the cases occurring in these two age groups were diagnosed at an earlier stage of the disease. In addition, examination of the temporal pattern exhibited by these cases shows that they were diagnosed in different years during 1987 to 1994.

No discernable geographic pattern or clustering of cases was observed in Shelburne. In addition, cases were not concentrated in any pattern that would suggest that an environmental factor had played a role in breast cancer incidence in Shelburne.

The majority of breast cancer cases in Shelburne were diagnosed at an early stage, rather than a later stage of the disease. Since breast cancer screening improves detection of breast cancer at an early stage of the disease, this finding suggests that women in Shelburne had access to and utilized breast cancer screening.

Shelburne displayed lower socioeconomic characteristics than the state of Massachusetts. This finding contradicts the research indicating that higher socioeconomic status is related to factors, which increase a women's risk of developing breast cancer. However, these socioeconomic markers describe the entire town of Shelburne and may not be representative of the study population.

In Shelburne, mean age at first full term pregnancy increased from 26 to 29 years and parity decreased from 1975 to 1990, primarily due to a decrease in first childbirths. These data suggest that reproductive factors that have been associated with an increased risk of breast cancer may have influenced the current rate of breast cancer in the area if the townwide experience is similar to that of cases included in this study.

VIII. RECOMMENDATIONS

In view of the fact that the statistically significant elevation in female breast cancer incidence observed in Shelburne during the time period 1982-1994 was due to an increase in incidence during the later period (1987-1994), the Community Assessment Unit will continue to monitor the incidence of breast cancer in this town.

Definitive information about the role of environmental factors in breast cancer is not currently available. However, studies are underway to evaluate potential links between breast cancer and environmental factors. The MDPH is currently conducting a large scale study on Cape Cod evaluating the role that environmental factors may have played in breast cancer incidence in that area. This work is being performed through a contract with the Silent Spring Institute. In addition, a second large-scale study is being conducted in Berkshire County where opportunities for exposure to PCBs have clearly occurred. If new information regarding the environment and breast cancer is gained through these research initiatives, the MDPH will consider this information and its relevance to the DRV community.

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D. Risk Factor Information for Selected Cancer Types

1. Cancers of the Brain and Central Nervous System

The nervous system consists of the central nervous system (CNS) which includes the brain and spinal cord, and the peripheral nervous system [NCI 1996]. Nine of ten nervous system cancers occur in or around the brain. Brain cancers usually do not spread out of the central nervous system, but cancers from other sites frequently metastasize or spread to the brain. These tumors would not be considered primary tumors of the brain or CNS because they originated in other parts of the body [NCI 1996].

Brain Cancer

Little is known regarding the etiology or causes of brain cancer. About 52 % of primary brain tumors in adults are glioblastomas, 18 % meningiomas, and 10 % astrocytomas [Higginson et al. 1992]. Among children, brain cancer is the second most common cancer.

Risk factor information for brain cancers varies depending on the histology (or cell type) of the cancer. Sixteen percent of those with primary brain tumors have a family history of this cancer [Black 1991b]. There are many different histologic types of brain cancer. The most common is glioma, which consists of astrocytoma & glioblastoma histologies. Astrocytoma has been associated with the development of multiple sclerosis in adults and exposure to lead in children. Glioblastoma has been associated with several viruses and occupational exposure to vinyl chloride. Some studies have noted a genetic pattern or familial tendency to develop gliomas (glioblastomas and astrocytomas are both gliomas). Most commonly documented is the occurrence of glioblastoma among families [Farwell and Flannery 1984; Mauron et al. 1984; Salcman and Solomon 1984]. Both astrocytoma and glioblastoma have been associated with cranial irradiation. Other factors that may be related to brain cancer include high-dose x-rays (e.g., prenatal x-ray exposures may lead to brain tumors)[Higginson et al. 1992], consumption of sodium nitrate (meat preservative), head trauma, exposure to some occupations (e.g., refinery of crude oil and production of petroleum-based chemicals, nuclear fuels and weapons industry, farmers, manufacture of synthetic rubber and polyvinyl chloride)[NCI 1996], and the use of barbiturates by pregnant women and by children [Page and Asire 1985].

Meningioma is a slow growing, usually benign tumor which has a high survival rate. Suspected risk factors in the development of meningiomas include previous head trauma (including injury and surgery), hormonal factors, certain genetic disorders, and exposure to some chemicals [Black 1991b].

The human data for the relationship between brain cancer and ionizing radiation are derived from studies of populations exposed prenatally to diagnostic x-rays (see above) and populations exposed postnatally to therapeutic x-rays or atomic bomb radiation [BEIR 1990]. These radiation-related reports include increased risk of brain tumors in children who received scalp radiation for tinea capitis in Israel and other x-ray treatments of head and neck during childhood [BEIR 1990], increased risks reported for workers in a nuclear fuel fabrication plant [Higginson et al. 1992], and increased risk of meningiomas (which are mostly benign brain tumors) with early exposures to dental x-rays [BEIR 1990].

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Colorectal Cancer

Colorectal cancer is the second most frequently diagnosed cancer type in the United States among males and females combined [ACS 1996, NCI 1996]. Among men and women individually, colorectal cancer is the third most frequently diagnosed cancer type in the United States, and in Massachusetts ranks second among females and third among males [NCI 1996]. Colorectal cancer incidence rises sharply after the age of 50, with a median age at diagnosis of 70 for men and 73 for women [NCI 1996]. Advances in diagnostic techniques have contributed to earlier diagnosis, and the use of endoscopy has been shown to lower the risk of developing cancer of the colon and rectum and to have contributed to the decrease in nation-wide incidence during the 1980's [Devesa 1995].

The major risk factor for cancer of the colon and rectum is a diet high in fat, particularly saturated fat (including red meats such as beef, pork or lamb, milk and milk products, oils, butter and margarine) and low in fiber (e.g., fresh fruits and vegetables) [Schottenfeld and Fraumeni 1996, NCI 1996]. Alcohol consumption also appears to be a risk factor for colorectal cancer [Schottenfeld and Fraumeni 1996, Giovannucci et al 1994]. The consumption of beer has been identified as a risk factor for rectal cancer [Schottenfeld and Fraumeni 1996]. Recent studies have found a strong association between long-term smokers and the development of colorectal cancer [Schottenfeld and Fraumeni 1996, Giovannucci et al 1994a, Giovannucci et al 1994b]. Other studies have also observed a significant relationship for individuals who consumed both tobacco and alcohol and developed colorectal polyps [Martinez et al 1995].

Chronic inflammatory diseases of the colon appear to increase the risk of developing colorectal cancer [Schottenfeld and Fraumeni 1996]. Inflammatory bowel disease (IBD) includes two separate types of chronic inflammatory disease: ulcerative colitis and Crohn's disease. The increased risk of developing colorectal cancer in patients with IBD has been estimated between 4 and 20 times greater than for a person without IBD. In addition, the mean age at diagnosis of

colorectal cancer in patients with IBD is about 20-30 years younger than the mean age of those without IBD and who develop colorectal cancer [Schottenfeld and Fraumeni 1996]. A family history of colon or rectal cancer, and conditions such as familial polyposis and Gardner's syndrome, measurably increase an individual's risk of developing colorectal cancer [Schottenfeld and Fraumeni 1996]. Women with colorectal cancer are at increased risk of developing independently occurring cancers of the breast, uterus, and ovary [Schottenfeld and Fraumeni 1996].

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Prostate Cancer

Cancer of the prostate is one of the most commonly diagnosed cancers among men in the United States and is primarily a disease of aging and/or elderly men [NCI 1996, ACS 1996]. Prostate cancer incidence increases with age. The median age at diagnosis is 72, and 82% of prostate cancer cases are diagnosed in men over age 65 [ACS 1996, NCI 1996]. Increasing prostate cancer incidence appears related to changes in diagnostic methods, such as serum testing for prostate-specific antigen PSA, which has led to increased detection at earlier stages [Devesa et al 1995, ACS 1996, NCI 1996]. By the late 1980's, prostate cancer became the most commonly diagnosed malignancy among U.S. men [Devesa et al 1995].

Prostate cancer rates are greater in countries where the population consumes more animal fat [Devesa et al 1995, NCI 1996, Schottenfeld and Fraumeni 1996]. Prostate growth depends on the hormone testosterone and some studies have suggested that a diet high in animal fats also increases the levels of this hormone, which may elevate the risk for prostate cancer [Schottenfeld and Fraumeni 1996]. In several large cohort and case-control studies, overweight men (defined as >30% above ideal body weight) had approximately 2.5 to 4.4 times the risk of developing prostate cancer than men who were near their desirable weight [Schottenfeld and Fraumeni 1996].

Additional risk factors for prostate cancer include a higher prevalence of past venereal disease, as shown in several large epidemiologic studies [Schottenfeld and Fraumeni 1996]. Family history

of prostate cancer also elevates an individuals risk of developing this disease [Schottenfeld and Fraumeni 1996].

Occupations which may related to the development of prostate cancer include some which are related to cadmium exposure (e.g., welding, electroplating, and alkaline battery production), however, several subsequent studies have been unable to confirm this risk [Schottenfeld and Fraumeni 1996].

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